

**A Better Starting Point in Life –
The Development of Children Born to Mothers Who Have Received
Treatment for Their Substance Abuse Problems While Pregnant**

A prospective follow-up study from pregnancy to 4½ years with multiple comparison groups

Philosophiae doctor (PhD) thesis

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2015

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*Series of dissertations submitted to the
Faculty of Social Sciences, University of Oslo
No. 535*

ISSN 1504-3991

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Cover: Hanne Baadsgaard Utigard.

Printed in Norway: AIT Oslo AS.

Produced in co-operation with Akademika publishing, Oslo.

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LIST OF CONTENTS

ACKNOWLEDGEMENTS	6
ABBREVIATIONS	8
SUMMARY	9
LIST OF PAPERS	11
Paper I.....	11
Paper II	11
Paper III	11
1 BACKGROUND/INTRODUCTION	12
1.1 Children of mothers with substance abuse problems	13
1.1.2 Short- and long-term child outcomes associated with prenatal substance exposure	13
1.1.3 Maternal substance abuse and child cognitive and social-emotional functioning...	15
1.2 Socio-demographic risk factors associated with maternal substance abuse and comorbidity with mental health problems	16
1.3 Treatment options for pregnant women with substance abuse problems in Norway...	19
1.4 Child outcome when mothers have received treatment for their substance abuse problems	20
2 THE PRESENT STUDY	21
2.1 Main research objectives	21
2.2 Design.....	22
3 MATERIALS AND METHODS	23
3.1 Participants	23
3.2 The present sample	25
3.3 Ethical Considerations	26
3.4 Materials and Measures	27
Figure 1 Measures from pregnancy until 4½ years of age	27
3.4.1 Measures during pregnancy (Papers I, II and III)	27
3.4.1.1 Substance use	27
3.4.1.2 Maternal mental health and personality traits	28
3.4.2. Measures at birth (Papers I and III)	29
3.4.2.1 Neonatal data.....	29
3.4.2.2 Meconium samples.....	29
3.4.3 Measures at infant age of 3 months (Paper II).....	29
3.4.4 Measures at 12 months (Paper II)	30

3.4.5 Measures at 2 years (Paper II).....	30
3.4.6 Measures at 4½ years (Paper III)	31
3.4.6.1 Child cognitive functioning.....	31
3.4.6.2 Child social-emotional functioning	31
3.4.6.3 Maternal/caregiver symptoms of anxiety and depression	32
3.4.6.4 Demographic characteristics and substance use at child age 4½ years.....	32
3.5 Statistical Analyses	33
3.5.1 Paper I: The perinatal outcome of children born to women with substance dependence detoxified in residential treatment during pregnancy.....	33
3.5.2 Paper II: Mother–Child Interaction and Early Language Skills in Children Born to Mothers with Substance Abuse and Psychiatric Problems	33
3.5.3 Paper III: Cognitive and Social-emotional Functioning at 4½ Years in Children Born to Mothers who have Received Treatment for Substance Abuse Problems while Pregnant	34
3.5.4 Statistical considerations.....	35
3.5.4.1 Missing data	36
3.5.4.2 Causality	36
3.5.4.3 Small sample sizes, statistical power and Type II error	36
3.5.5 Statistical software	37
4 SUMMARIES OF PAPERS	37
4.1 Paper I: The perinatal outcome of children born to women with substance dependence detoxified in residential treatment during pregnancy.....	37
Aims	37
Methods.....	37
Main results.....	37
4.2 Paper II: Mother–Child Interaction and Early Language Skills in Children Born to Mothers with Substance Abuse and Psychiatric Problems.....	38
Aims	38
Methods.....	38
Main results.....	38
4.3 Paper III: Cognitive and Social-emotional Functioning at 4½ Years in Children Born to Mothers who have Received Treatment for Substance Abuse Problems while Pregnant....	39
Aims	39
Methods.....	39
Main results.....	39
5 DISCUSSION	41
5.1 Summary of main results	41

5.2 Interpretation and discussion of the findings.....	42
5.2.1 Maternal characteristics and mental health problems	42
5.2.2 Infant perinatal outcome	45
5.2.3 Group differences and predictors of language skills at age 2 years	46
5.2.4 Cognitive and social-emotional functioning at age 4½ years	48
5.2.5 Foster placements by the age of 4½ years	51
5.3 Methodological considerations.....	52
5.3.1 Sample size	52
5.3.2 Recruitment and selection bias	53
5.3.3 Missing data and attrition bias	53
5.3.4 Cross-cultural considerations.....	54
5.3.5 Objectivity in observation and assessment	54
5.3.6 Direct effects and confounding variables or a complex field and multiple transactions	56
5.4 Clinical implications.....	57
5.5 Future perspectives	59
6 CONCLUSIONS.....	60
REFERENCES.....	61

ACKNOWLEDGEMENTS

The present study was conducted at the National Network for Infant Mental Health, RBUP, Eastern and Southern Norway, and funding was provided by The Norwegian Research Council and contributions from RBUP.

This thesis is not a solo project. To each of you who have supported me throughout the process and contributed to the accomplishment of this thesis, I am very grateful.

Firstly, I am most thankful to the mothers, caregivers and children who participated in the study for taking their time to come to multiple assessments, filling out many questionnaires over the years and for sharing their valuable experiences. I also wish to express my gratitude to our collaborators at the residential treatment institutions for substance abuse throughout Norway, for taking part in the recruitment of mothers with substance abuse problems and in the data collection. Many thanks as well to the clinicians at the out-treatment institutions for women with mental health problems for contributing to recruitment to the high-risk comparison group.

I also want to thank my three supervisors. To my first supervisor, Vibeke Moe: Thank you for always having been there for me when I needed help, for your calmness, for your impressively continuous good mood and humor, for encouraging me to seek relevant knowledge and for sharing your vast knowledge and expertise of infants at risk. To my second supervisor, Kristine Walhovd: You have played a particularly important part in my journey of learning to write scientific articles and understanding the publication process, as well as in the statistical analyses, thank you for being so generous, for sharing your vast experience, for always being to-the-point, and for your efficiency. To my third supervisor, Kari Slinning: Thank you for your warm support, for your questions and reflections, for sharing your knowledge and for always showing an interest in my work.

I also want to express my gratitude to my coauthors for their important contributions and insightful comments on the papers, and my research coworkers. To Torill Siqveland: you have always been so attentive and kind, thank you for sharing your experience, knowledge and thoughts with me during these years, I am immensely grateful. To Astrid Bjørnebekk: your positive attitude made the data collection period enjoyable and interesting, and I very much appreciated the time we worked together. To Lars Smith: thank you for your time, for your constructive feedback and for sharing your immense knowledge of developmental psychology. To Tore Wentzel-Larsen: thank you for helping me and guiding me through the statistical analyses, and for always being available when I had any questions. To Egil Nygaard: Thank you for your thorough and critical reflections. I also wish to thank Anders

Martin Fjell for valuable comments and advice concerning the research project, and Håkon Grydeland who stepped in during the data collection period. A warm thanks also to Bibbi Juell for her important contribution in recruitment and staying in contact with all the families who participated in the research project. I also wish to thank Meike Meier and Rigmor Grette Moe for their thorough scorings of all the mother-infant interaction recordings.

A warm thanks also to all my colleagues at the National Network for Infant Mental Health at RBUP. I have truly enjoyed being part of this group of highly competent researchers and clinicians from whom I have learned so much during the entire process of writing this thesis. A special thanks to Marit Bergum Hansen, who most generously lent me her office when I needed a quiet place to write and who provided me with good conditions at work.

Finally, I want to thank my family and all my friends who have been cheering for me the whole long way, your support has meant so much to me. Lastly, I am greatly thankful to my wonderful husband, Aleksander, whose encouragement and interest in my work have inspired and motivated me during the whole process, and our three children Ola, Johan and Jenny, who patiently and sometimes impatiently have been there and reminded me of what is truly important in my life.

ABBREVIATIONS

ANOVA	Analysis of Variance
ASEBA	Achenbach System of Empirically Based Assessment
CBCL	Child Behavior Check List
CPS	Child Protection Service
EPDS	Edinburgh Postnatal Depression Scale
EuropASI	European Addiction Severity Index Questionnaire
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorder
MCMI- III	Millon's Clinical Multiaxial Inventory, third edition
MRI	Magnetic Resonance Imaging
MSEL	Mullen Scales of Early Learning
NAS	Neonatal Abstinence Syndrome
PCERA	Parent-Child Early Relational Assessment
SCL-25	Hopkins Symptom Check List, short version
TRF	Teachers Report Form
WPPSI-III	Wechsler Preschool and Primary Scale of Intelligence, third edition

SUMMARY

This prospective, follow-up study follows children born to mothers with opioid- and poly-substance abuse problems who have received help for their substance abuse problems while pregnant. The main objective of this thesis was to contribute to the understanding of the development of children born to mothers with a history of substance abuse problems and gain more knowledge about relevant risk and protective factors associated with their cognitive and social-emotional functioning.

The mothers in the study group were recruited during pregnancy from residential treatment institutions in Norway where they received treatment for substance abuse problems and underwent detoxification if they were currently abusing substances. Because substance abuse and mental health problems often co-exist and are often confounded in substance-abuse research, the study included two concurrent comparison groups, one group of children and their mothers with who had mental health problems, but not substance abuse problems, and one low-risk group of children and mothers with neither mental health nor substance abuse problems. The present thesis also included two additional comparison groups from an earlier time cohort recruited between 1991 and 1996 in Norway, one group of children and their mothers who had abused substances throughout their pregnancies (no such treatment was available at that time), and one low-risk comparison group from the same time with children and their mothers without substance abuse problems.

The results revealed that the infants born to mothers who underwent detoxification during pregnancy demonstrated better perinatal outcomes on gestational age and head circumference, as well as no NAS, compared to the infants in the earlier time cohort whose mothers were not in residential treatment. Additionally, no miscarriages, complications or morbidities were associated with residential detoxification treatment.

The mothers who received treatment for their substance abuse problems were younger, they had a lower educational level and were more likely to be single compared to the two concurrent comparison groups of mothers. They scored higher on antisocial personality traits in pregnancy and on observer-rated intrusiveness and lack of sensitivity in interaction with their 1-year-old children than both the two concurrent comparison groups, though not when controlling for maternal age, education and single parenthood. The children in the study group scored significantly lower on expressive language at 2 years of age than the low-risk comparison children, but not when controlling for maternal age, education and single parenthood. Maternal intrusiveness observed in mother-child interaction at 12 months was

significantly related to child expressive language skills at 2 years, also when controlling for socio-demographic risk factors.

The results further showed no significant group differences in cognitive functioning at 4½ years of age. However, the children in the study group showed, albeit mostly below the clinical threshold, significantly more caregiver-rated internalizing and total problems on the Child Behavior Check List than the low-risk comparison children at 4½ years of age, and similar to that of the high-risk comparison children. Caregivers' present symptoms of anxiety and depression were related to ratings of child total behavior problems. Birth weight showed an effect on internalizing problems at 4½ years, and partly mediated the relationship between group and social-emotional problems, but not when controlling for caregiver socio-demographic risk factors such as lower education, single parenthood and current caregiver symptoms of anxiety and depression.

At the 4½-year follow-up, seven (31.8%) of the children from the study group had been foster placed. When excluding the foster children from the analyses, the difference in birth weight and internalizing problems between the children in the study group and the low-risk comparison children was significantly reduced.

The results suggest that the children born to mothers with substance abuse problems who were detoxified while pregnant were born with a smaller biomedical vulnerability and a better starting point in life, possibly explained by lower levels of prenatal substance exposure, better nutrition and prenatal care and supportive follow-up after birth relative to other samples. At the same time, maternal psychopathology, maternal intrusiveness in interaction, not to mention socio-demographic risk factors, may influence the development of early language skills, as well as the development of social-emotional difficulties in children born to mothers with a history of substance abuse problems. The findings imply that in addition to optimizing prenatal factors by admittance to residential care units with maternal detoxification, good and stable nutrition and psychosocial treatment during pregnancy, families with a history of substance abuse and their children are in need of long-term follow-up and support. Interventions with focus on sensitive caregiving and developmental supportive parenting behavior, as well as the caregivers' mental health problems, should be applied in order to promote expressive language skills, enhance further positive cognitive development and prevent development of social-emotional problems in children born to mothers who have received help with their substance abuse problems while pregnant. The results further suggest that the children placed in foster care may be in particular need of long-term follow-up, together with their new families.

LIST OF PAPERS

Paper I

Haabrekke, K. J., Slinning, K., Walhovd, K. B., Wentzel-Larsen, T., & Moe, V. (2014). The perinatal outcome of children born to women with substance dependence detoxified in residential treatment during pregnancy. *Journal of Addictive Diseases*, 33(2), 114-123. doi: 10.1080/10550887.2014.909698

Paper II

Haabrekke, K. J., Siqueland, T., Smith, L., Wentzel-Larsen, T., Walhovd, K. B., & Moe, V. (2014). Mother–Child Interaction and Early Language Skills in Children Born to Mothers with Substance Abuse and Psychiatric Problems. *Child Psychiatry and Human Development*, 1-13. doi: 10.1007/s10578-014-0512-0

Paper III

Haabrekke, K. J., Siqueland, T., Nygaard, E., Bjornebekk, A., Slinning, K., Wentzel-Larsen, T., Walhovd, K. B., Smith, L., & Moe, V. (submitted). Cognitive and Social-emotional Functioning at 4½ Years in Children Born to Mothers who have Received Treatment for Substance Abuse Problems while Pregnant. *Child Psychiatry & Human Development*.

1 BACKGROUND/INTRODUCTION

Substance abuse is an increasing problem in society, to the person with a substance abuse problem and the affected people in close surroundings. Alcohol is the most commonly used substance in many countries throughout the world, and it is reported that approximately one in 16 European adults suffer from alcohol dependence in any given year (World Health Organization, 2012). An estimated 8.2% of men and 3% of women in Norway have an alcohol abuse problem (Norwegian Institute of Public Health, 2011). It is difficult to obtain exact numbers of prevalence of illicit substance use; consequently, the following numbers are based on estimates: There were approximately 1.3 million opioid users in the European countries in 2012 (European Monitoring Centre for Drugs and Drug Addiction, 2014), while 34% of these were women in which the majority were of childbearing age. In Europe, multiple substances are generally used concomitantly. Levels of lifetime prevalence of illicit substance use vary considerably between the European countries, from approximately one-third of adults in Denmark, France and the United Kingdom, to less than one in 10 in Bulgaria, Greece, Cyprus, Hungary, Portugal, Romania and Turkey (European Monitoring Centre for Drugs and Drug Addiction, 2014).

In Norway in 2013, the Norwegian Institute for Alcohol and Drug Research conducted a survey based on a phone interview, with a representative sample drawn from the population register. It had a response rate of 57.3%, and there were 2,101 respondents. A total of 1,790 were in the 16–64 age group. Numbers from this survey estimated that cannabis is by far the most common illegal drug used in Norway, with the lifetime prevalence rate being 23.3%. For cocaine, the lifetime prevalence was estimated to be 4.2%, for amphetamines 3.7%, for ecstasy 2.3%, for LSD 1.5%, for GHB/GBL 1.1% and for heroin 0.7%. The lifetime prevalence for all illegal substances other than cannabis was about twice as high for males than for females. Among females between 16 to 34 years, the lifetime prevalence for cannabis-use was 23.5%, for cocaine it was 4.1%, for amphetamines it was 3.7% and for ecstasy it was 2.5%. For heroin, GHB/BGL and LSD, the lifetime prevalence for women between 16 and 34 years was so small that it was not statistically significantly different from zero in this drawn sample ($p > .05$) (Norwegian Institute for Alcohol and Drug Research (SIRUS), 2015). However, a study carried out in 2013 among 1,020 people with substance abuse problems recruited in or outside various low-threshold services, and on the street from seven Norwegian cities, reported that 43% had injected heroin and 19% had smoked heroin during the previous four weeks (Gjersing & Sandøy, 2014).

1.1 Children of mothers with substance abuse problems

An estimated 10% of children in the EU and 8.3% of Norwegian children live in families adversely affected by alcohol (McNeill, 1998; Norwegian Institute of Public Health, 2011). There are also a considerable number of women with illicit substance abuse problems of childbearing age. An estimated 30,000 children are born every year in Europe to mothers who have opiate abuse problems, and the number of pregnant women who have poly-substance abuse problems may be equally as high (Gyarmathy et al., 2009). Every year in Norway, an unknown number of children grow up in families with illicit substance abuse problems. It is well documented that substance abuse problems and mental health problems often occur together (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997; Kessler et al., 1997; Verheul, 2001). Depending on the degree of severity (from more severe diagnoses of psychosis or schizophrenia to a single depressive episode), it has been estimated that between 10 to 37% of Norwegian children live with parents who have mental health problems. In 2013, the Norwegian Child Protection Service (CPS) reported 2,122 new cases of children living in families with parental mental health problems, where these problems affected the parents' caregiving in such a way that the CPS had to take action (Statistics Norway, 2015b). This translates to approximately 0.21% of the Norwegian child population, thus implying that few of the estimated children living with parents with mental health problems are noticed and receive help. The number may be equally low for children with parents with substance abuse problems; the CPS reported 1,329 new cases of children in 2013 where there was parental substance abuse (Statistics Norway, 2015b), while it is likely that a much larger number of children grow up with parents with substance abuse problems.

1.1.2 Short- and long-term child outcomes associated with prenatal substance exposure

Maternal substance abuse poses a great risk of negative effects on both the pre- and postnatal development of the child. Maternal use of licit substances such as alcohol and nicotine, as well as illicit substances such as opioids, amphetamines, cannabis and cocaine, transfer through the placenta and enter the bloodstream of the fetus. Prenatal exposure to substances interferes with the formation of neurons and may disturb fetal brain development (Harlan & Song, 1994; Hellström-Lindahl, Seiger, Kjaeldgaard, & Nordberg, 2001; Hu, Sheng, Lokensgard, & Peterson, 2002; Willoughby, Sheard, Nash, & Rovet, 2008).

The adverse effects of prenatal alcohol exposure are especially well documented, and represent a spectrum of physiological anomalies and disturbances in the neurocognitive and behavioral development of the child (Flak et al., 2014; Niclasen, Andersen, Strandberg-

Larsen, & Teasdale, 2014). Alcohol consumption during pregnancy increases the risk of Fetal Alcohol Spectrum Disorder (FASD), with Fetal Alcohol Syndrome (FAS) as the most severe consequence in newborns (Barr & Streissguth, 2001). The term *fetal alcohol spectrum disorder* illustrates how prenatal alcohol exposure may show its effects within a wide spectrum of symptoms (Dörrie, Föcker, Freunscht, & Hebebrand, 2014; Hoyme et al., 2005; Riley & McGee, 2005; Sokol, Delaney-Black, & Nordstrom, 2003; Streissguth, 1992). In Norway, an unknown number of children are born with FASD, but estimates based on international numbers suggest that it may be several hundred every year (Moe, Siqueland, & Slinning, 2011).

Maternal smoking in pregnancy is a known cause of reduced infant birth weight, preterm delivery and miscarriage (Abel, 1980; England et al., 2001; Persson, Grennert, Gennser, & Kullander, 1978; Secker-Walker, Vacek, Flynn, & Mead, 1998; Shah & Bracken, 2000). Because of the well-known adverse effects of prenatal exposure to alcohol and nicotine, many European countries have had state-funded campaigns to prevent pregnant women from drinking and smoking during pregnancy.

The use of illicit substances and the effects of prenatal substance exposure on child development are less studied compared to the effects of alcohol. Prenatal exposure to opioids has been associated with a lower birth weight and gestational age, reduced head circumference and Neonatal Abstinence Syndrome (NAS) (Bakstad, Sarfi, Welle-Strand, & Ravndal, 2009; Konijnenberg & Melinder, 2014b; Moe & Slinning, 2001; Rosen & Johnson, 1985). NAS is a constellation of signs and symptoms that indicate an irritability of the autonomic nervous system and dysfunction in the gastrointestinal tract and respiratory system of the infant. Newborns born with NAS experience severe regulation problems and are in need of long, often medically complex and costly hospitalizations (Jones et al., 2005; Kaltenbach, Berghella, & Finnegan, 1998), and NAS may be life threatening if not treated (Hans & Jeremy, 2001). In the United States, there has been a threefold increase in newborns with NAS the past 10 years (Patrick et al., 2012). In Norway, there have been systematic registrations of newborns with NAS from 1999, and the numbers have increased every year, from 22 infants with NAS in 1999 to 73 in 2011. These numbers include both infants born to mothers in Opioid Maintenance Treatment (OMT) and to mothers with illicit substance abuse during pregnancy. Approximately 40 Norwegian children are born every year to women enrolled in an OMT program, and it has been reported that 60% of these newborns have had withdrawal symptoms after birth that require treatment (Bakstad et al., 2009). It remains uncertain as to whether NAS in itself is related to later problems in child functioning,

although a relationship between NAS in methadone-exposed infants and later problems with visual attention has been documented (Konijnenberg & Melinder, 2014b).

A lower birth weight and gestational age have been associated with a variety of other adverse prenatal environmental conditions in addition to prenatal substance exposure, such as cigarette smoking and under- or malnutrition, as well as maternal psychological stress, anxiety and depression (England et al., 2001; Glover, 2014; Hedegaard, Henriksen, Sabroe, & Secher, 1993; Moe & Slinning, 2001; Secker-Walker et al., 1998). However, a lower birth weight in opioid-exposed infants has also been found after controlling for gestational age and other adverse conditions such as maternal alcohol use, smoking, malnutrition and socio-demographic risk factors (Creanga et al., 2012; Mactier, Shipton, Dryden, & Tappin, 2014). Furthermore, a lower birth weight and gestational age have been found to predict poor cognitive and social-emotional functioning in childhood (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Hediger, Overpeck, Ruan, & Troendle, 2002; Monk, Spicer, & Champagne, 2012; Shah, Robbins, Coelho, & Poehlmann, 2013).

1.1.3 Maternal substance abuse and child cognitive and social-emotional functioning

There is a growing literature showing that infants prenatally exposed to poly-substances may have an increased risk of short and long-term neurodevelopmental difficulties. Studies of children born to mothers with cocaine abuse problems have found an increased risk of delayed language development (Bandstra et al., 2002; Delaney-Black et al., 2000; Lewis et al., 2004; van Baar & de Graaff, 1994), as well as deficits in visuo-spatial skills, working memory and executive functioning (Mayes, Snyder, Langlois, & Hunter, 2007; Singer et al., 2004). Prenatal marijuana exposure has been related to later deficits in visual and attentional functions (Fried & Smith, 2001), whereas prenatal nicotine exposure has been found to predict learning and memory problems through childhood and adolescence (Cornelius, Ryan, Day, Goldschmidt, & Willford, 2001). Opioid exposure during pregnancy, both illicitly through heroin and medically through methadone, have been found to be related to later problems in executive functioning, visuospatial and perceptual skills and motorical skills (Hans & Jeremy, 2001; Konijnenberg & Melinder, 2014a; McGlone et al., 2014; Melinder, Konijnenberg, & Sarfi, 2013; Moe, 2002; Ornoy, Segal, Bar-Hamburger, & Greenbaum, 2001). Although the causal mechanisms behind these are complex and debated, both animal models and human fetal cell culture studies point to direct neurotoxic effects of opioids (Harlan & Song, 1994; Hu et al., 2002; Wang & Han, 2009). Furthermore, Magnetic Resonance Imaging (MRI) studies have shown smaller neuroanatomical brain volumes in

children prenatally exposed to opioids and other substances (Walhovd et al., 2007; Yuan et al., 2014), as well as differences in white-matter characteristics compared to controls (Walhovd et al., 2010).

Several studies have documented that children prenatally exposed to substances also have been shown to struggle with various aspects of social-emotional functioning. Prenatal exposure to opioids, cocaine and poly-substances have been associated with early regulation problems in infants, in addition to later internalizing and externalizing difficulties (de Cubas & Field, 1993; Goldschmidt, Day, & Richardson, 2000; Hans, 1996; Hans & Jeremy, 2001; Konijnenberg & Melinder, 2014a; Rosen & Johnson, 1985; Slinning, 2004). Some studies have found children prenatally exposed to opioids or poly-substances in utero to be at greater risk for problems with behavioral and emotional regulation (Lester & Lagasse, 2010), which includes aggression or behavioral problems (de Cubas & Field, 1993; Hans, 1996), attentional difficulties (Davis & Templer, 1988; Slinning, 2004) and ADHD symptoms (Hans, 1996; Ornoy et al., 2010; Ornoy, Segal, Bar-Hamburger, & Greenbaum, 2001).

1.2 Socio-demographic risk factors associated with maternal substance abuse and comorbidity with mental health problems

Common to many studies of outcomes in children born to mothers with substance abuse problems is the challenge of disentangling the various possible effects, and what has been described as confounders in research on these children (Tronick & Beeghly, 1999). Over the past decades, it has been recognized that in addition to knowledge about the direct teratogenic effects and mechanisms of prenatal substance exposure, the various other negative factors associated with maternal substance abuse must be taken into account to an extent beyond looking at these factors as confounding variables.

It must be recognized that maternal substance abuse problems is often a marker for several environmental and psychosocial adversities. It is well known that maternal substance abuse problems often coexist with a lower education and income, single parenthood and poor social network (Beeghly & Tronick, 1994; Hans & Jeremy, 2001; Irner, Teasdale, Nielsen, Vedal, & Olofsson, 2012). Moreover, these mothers often experience relational difficulties and psychosocial problems (Pajulo, Suchman, Kalland, & Mayes, 2006; Suchman, McMahon, Slade, & Luthar, 2005). Comorbidity between maternal substance abuse problems and various psychiatric disorders is well documented (Espinosa, Beckwith, Howard, Tyler, & Swanson, 2001; Hans, Bernstein, & Henson, 1999; Luthar, Cushing, Merikangas, & Rounsaville, 1998;

Pajulo et al., 2011; Verheul, 2001), with personality disorders such as antisocial- and borderline personality being especially prevalent (Haller, Knisely, Dawson, & Schnoll, 1993).

When considering all the coexisting problems associated with maternal substance abuse, it is evident that prenatal substance exposure is not the only risk factor potentially exerting an influence on a child's development. Maternal negative childhood experiences, current lifestyle and psychological problems may compromise the mothers' caregiving abilities, and potentially influence the children's development in a negative direction independent of or in addition to prenatal substance exposure. A relationship between maternal postnatal depression and delayed child language development has been documented (Lovejoy, Graczyk, O'Hare, & Neuman, 2000; Schjolberg, Eadie, Zachrisson, Oyen, & Prior, 2011), with maternal caregiving as a mediating factor (Stein, Malmberg, Sylva, Barnes, & Leach, 2008). In combination with psychiatric problems and other psychosocial difficulties, mothers with substance abuse problems often experience caregiving as a challenging task, as they may have a reduced capacity to read, interpret and contingently respond to the infant's signals and ways of communication (Beeghly & Tronick, 1994; Pajulo et al., 2012; Suchman, Pajulo, Decoste, & Mayes, 2006). They have also been shown to be less sensitive, more intrusive and display more harshness in interacting with their infants (Eiden, Schuetze, Colder, & Veira, 2011; Pajulo et al., 2011; Pajulo et al., 2001; Siqveland, Smith, & Moe, 2012). Maternal harshness and insensitivity may again be associated with comorbid psychopathology, particularly through the symptoms of antisocial personality and other personality disorders (Hans et al., 1999). Personality disorders may themselves be closely related to additional risk factors, including relational difficulties, low education and single parenthood (Serbin & Karp, 2004). A potential biological vulnerability of the infant due to prenatal substance exposure, and further difficulties in self-regulation, combined with maternal background factors such as aversive relational experience and distress, may together contribute to negative patterns in the mother-infant interaction (Eiden, Schuetze, & Coles, 2011; Siqveland, Olafsen, & Moe, 2013; Siqveland et al., 2012). Negativity in the mother-infant interaction may further contribute to problems in the child's later social-emotional functioning (Eiden, Schuetze, Veira, et al., 2011).

It is clearly a challenge to separate direct teratogenic and other prenatal effects from those of the postnatal environment in cases in which substance-exposed children grow up with their biological parents, as these risk factors may interact in affecting developmental outcomes. Cumulative environmental risk, including aspects of the caregiving conditions such as maternal insensitivity, maternal psychiatric problems and difficult psychosocial life

circumstances, may together with a potential biomedical vulnerability in the child, account for the observed variations in cognitive and social-emotional development in children growing up with mothers with substance abuse and psychiatric problems. These children may experience both prenatal and postnatal risks that could compromise their development. When investigating developmental outcomes of children born to mothers with substance abuse problems, the child's caregiving environment not to mention maternal psychiatric problems and other psychosocial challenges such as single parenthood and low education, are all important factors in addition to prenatal substance exposure (Marcus, Hans, & Jeremy, 1984; Tronick & Beeghly, 1999).

Interactions between child and caregiver factors influencing each other over time can be understood through the transactional model (Sameroff, 1990; Sameroff & Chandler, 1975). This model emphasizes that a child's development is a result of a continually dynamic process between the child and its caregiving environment, in which both the child and the caregiving environment are equally important. The child cannot be understood without the caregiving environment and the caregiving environment cannot be understood without the child, because they influence one another. A child with a biomedical vulnerability caused by prenatal substance exposure and other adverse prenatal factors is in particular need of a sensitive caregiving environment in order to recover from abstinence and achieve a stable regulation system. Because of her negative life experiences and comorbid psychopathology, a mother with substance abuse problems may be less capable of providing her vulnerable child with a sensitive and stimulating caregiving environment. When caring for an infant who has been born with NAS and might have regulation disturbances, a mother may have feelings of guilt and other negative emotions such as irritability and frustration, which are difficult for her to handle. These feelings may influence her caregiving capacity, making her less sensitive and potentially reinforcing the regulation disturbance in her child, which again may lead to more maternal negative emotions. These mutual influences can become a negative spiral that may also be influenced and enlarged by additional distal factors such as low maternal education, lower income, less relational support and single parenting. Children born to mothers with substance abuse problems are therefore at multiple risk for adverse developmental outcomes, both through a biomedical vulnerability and a potentially less sensitive caregiving environment influencing one another over time.

1.3 Treatment options for pregnant women with substance abuse problems in Norway

In Norway, there are various treatment opportunities for pregnant women with substance dependence problems. One treatment option for opioid dependence is opioid maintenance treatment (OMT), and for pregnant women who are already enrolled in the OMT-program, it is recommended to continue the medication during pregnancy as it also is in many European countries and the United States (World Health Organization, 2009). There are also other treatment options for pregnant women with substance abuse problems. Several in-patient clinics for individuals with substance abuse problems in Norway specialize in medically supervised detoxification in a residential setting where pregnant women with untreated substance dependence get medical and psychological support in becoming drug-free during their pregnancies. Both pregnant women in OMT who wish to taper off and women with opiate and poly-substance abuse who are not in OMT can voluntarily obtain help in these residential clinics. Pregnant women with previous substance abuse, who are not currently using substances but fear relapse, can also receive help in the residential institutions. In addition, Norwegian legislation (cf. Social Service Law § 6–2a, replaced by the Act for Municipal Health and Care Services, Section 10-3 from January, 2012) authorizes the detention of pregnant substance using women in residential treatment in order to protect the fetus. This Act states that without her consent, a pregnant woman with substance abuse can be placed in an institution and be held there for the rest of her pregnancy if the abuse is of such a nature that it is probable that the child will be adversely affected. The purpose of this Act is to prevent and minimize the likelihood of injury to the child, and it can be put into practice if voluntary measures are insufficient. Another aim of the Act is to help the woman in enabling her to take care of her child after it is born. The number of pregnant women who are involuntarily institutionalized based on this Act varies, and in 2013 the number was 65 throughout Norway (Statistics Norway, 2015a). The residential treatment institutions in Norway are designed to meet each woman's individual state and situation, hence, the exact treatment in terms of medication, therapeutic intervention and other support will vary. What is common to all the Norwegian institutions that provide help for women with substance abuse problems is a very close monitoring and a supportive environment. While staying in residential care, the mothers, and in some cases their partner, live together in an environment with other families. They receive help and guidance from professional therapists concerning nutrition, housekeeping and economy, as well as mother-infant interaction and psychological treatment.

Some of the residential treatment institutions in Norway are designed to treat both voluntary and involuntary patients, while others treat only voluntary patients. The legislation that authorizes the detention of pregnant women with substance dependence problems came into existence in 1996. Since then, there have been great changes, and now several in-patient clinics specialize in the treatment of pregnant women with substance abuse problems throughout Norway. Besides one study reporting that infant birth weight increased with the number of days a women had been under involuntary treatment for substance abuse while pregnant (Nordlie, 2012), there is virtually no documentation on the short- and long-term outcome of the infants born to mothers who have received help for their substance abuse problems in residential institutions while pregnant.

1.4 Child outcome when mothers have received treatment for their substance abuse problems

It has been claimed that detoxification during pregnancy is hazardous to the fetus due to maternal and intrauterine abstinence and can result in miscarriage, though there is no clear evidence to support this view (Luty, Nikolaou, & Bearn, 2003; McCarthy, 2012). It has been a frequent finding that detoxification increases the risk of drop-out from treatment and relapse into drug abuse (Norwegian Directorate of Health, 2011), which may also result in overdose and death. However, studies reporting on abstinence and drop-out from treatment are based on outpatient treatment. There is little research investigating whether this is the case when the detoxification takes place in a residential setting. In addition, although receiving help with the substance abuse problems in residential institutions, the comorbid psychiatric problems and additional proximal environmental risk factors may still be present, thus potentially affecting the child's cognitive and social-emotional development. The increase in treatment options, in which mothers receive help in stopping their substance abuse, implies that mothers with a history of substance abuse problems have a greater opportunity to take care of their own children today compared to the early 1990s, when many children were taken into custody and raised in foster homes (Moe, 2002; Moe & Slinning, 2001; Slinning, 2004). A recent Norwegian study showed that children born to- and growing up with mothers in outpatient treatment, who stopped their substance abuse within the first trimester, had lower cognitive scores than low-risk comparisons, as well as children of long-term substance abusers growing up in foster care (Hjerkin, Lindbaek, Skogmo, & Rosvold, 2010). This finding may suggest that environmental risk factors are present, thereby possibly influencing the children's cognitive development.

There is a need for more knowledge about the relevant risk and protective factors associated with cognitive and social-emotional functioning in children growing up with mothers with a history of substance abuse. Findings may have important clinical implications in terms of recommendations for what type of treatment is best suited to attend to both the mothers with substance abuse problems and their children.

2 THE PRESENT STUDY

The study described in this thesis was part of a larger prospective longitudinal research project, which followed a group of children born to mothers with substance abuse problems from pregnancy to 4½ years of age. The mothers had received help for their substance abuse problems and were recruited from treatment institutions while pregnant. Because substance abuse and mental health problems often co-exist and are often confounded in substance abuse research, the present study includes two concurrent comparison groups: one group of children born to mothers with mental health problems, but no substance abuse problems (high-risk comparison group), and one group of children born to mothers with neither mental health nor substance abuse problems (low-risk comparison group). The original project was initiated in 2004, and the data collection took place from 2004 through 2012. The present thesis also includes two additional comparison groups from an earlier time cohort recruited between 1991 and 1996: one group of children born to mothers who had abused substances throughout their pregnancies because there were no such treatment available at that time, and one comparison group from the same time with children born to mothers without substance abuse problems.

2.1 Main research objectives

The main objective of this thesis was to contribute to the understanding of the development of children born to mothers who have received help for their substance abuse problems during pregnancy, and gain more knowledge about the relevant risk and protective factors associated with their later cognitive and social-emotional functioning.

The more specific research questions of this thesis were:

1. What characterizes the mothers who were in residential treatment for their substance abuse problems in terms of reported substance abuse, mental health problems and

socio-demographic risk factors in comparison to the high- and low-risk comparison groups? (Papers I, II and III)

2. Do the infants born to mothers who underwent detoxification in residential treatment during pregnancy have better perinatal outcomes in terms of NAS, birth weight, head circumference and gestational age compared to infants born to mothers when no such treatment was available? Moreover, will differences in perinatal outcomes between substance-exposed and low-risk comparison infants be smaller where the mothers have been in treatment? Is detoxification in a residential setting associated with an increased incidence of pregnancy complications, morbidities or miscarriages? (Paper I)
3. To what extent can prenatal substance exposure, maternal antisocial- and borderline personality traits, postnatal depression at 3 months and maternal intrusiveness in social interactions observed at 12 months predict expressive and receptive language skills at 2 years? Secondly, to what extent can such relationships be observed independently of socio-demographic factors, such as single parenthood and maternal education? Lastly, can maternal intrusiveness observed in the mother-infant interaction at 12 months be a mediating factor, linking maternal psychiatric symptoms and child language functioning at 2 years? (Paper II)
4. To what extent will the children born to mothers who received help for their substance abuse problems differ in cognitive and social-emotional functioning at 4½ years of age compared to children born to mothers with mental health problems and children of mothers with no such problems while pregnant? Can birth weight mediate the possible group differences in cognitive and social-emotional functioning at 4½ years, also when adjusting for caregiver characteristics such as single parenthood, low education and mental health problems? (Paper III)

2.2 Design

The design of this thesis is a naturalistic follow-up study with data collection at several time points, and in attempt to answer the research questions, multiple comparison groups were included. Data was collected at six time points: during pregnancy (Papers I, II, III), at birth

(Papers I, III), at an infant age of 3 months (Paper II), at 12 months (Paper II), at 2 years (Paper II) and at 4½ years of age (Paper III). In order to answer research question 1, the two concurrent comparison groups, both low- and high-risk, were included. In order to answer research question 2, the high- and low-risk comparison groups from the earlier time cohort were included, in addition to the concurrent low-risk comparison group. In order to answer research questions 3 and 4, the two concurrent comparison groups, both low- and high-risk, were included.

3 MATERIALS AND METHODS

3.1 Participants

The subjects of interest for this thesis were children born to mothers with substance abuse problems who received treatment in residential institutions during pregnancy. The women could either have had an ongoing- or previous history of substance abuse, and were recruited by clinicians serving as research co-workers from five different residential treatment institutions in Norway (Lade Treatment Center in Trondheim, Bergen Child- and Family Center, the Borgestad Clinic in Skien, Blåklokka in Førde and the Family Unit, Hov i Land). It was communicated to the research co-workers that all women admitted to treatment should be asked to participate in the study, and the women received both verbal and written communication about the research project. Thirty-seven mothers were originally recruited from the treatment institutions, but six mothers withdrew shortly after recruitment, so 31 mothers in all were included in the study group. All of the mothers with ongoing substance abuse while pregnant underwent detoxification as part of the residential treatment, though at various time points depending on when they were admitted to the institutions. A total of 26.9% of the mothers were admitted into treatment in their 1st trimester of pregnancy, 30.8% in their 2nd trimester and 34.6% in their 3rd trimester. See Papers I and II for detailed reports of substance abuse during pregnancy for this group. The exact treatment in terms of medication, therapeutic intervention and other support varied according to each admitted woman's individual condition and situation. What was common to the Norwegian institutions the women were recruited from is that they provided help through both a close monitoring and a supportive environment. The mothers, and in some cases their partners, lived together in an environment with other families. They received help and guidance from professional therapists concerning nutrition, housekeeping and economy, as well as psychological treatment. As described above, Norwegian legislation authorizes the detention of pregnant women with substance dependence problems in residential treatment in order to protect the

fetus. Of the 31 eligible women, eight (25.8%) were involuntarily institutionalized, whereas 23 (74.2%) women were in voluntarily treatment. There were two fraternal twins within this group, while the rest were singleton pregnancies.

The present study included multiple comparison groups, with one comparison group consisting of children and their mothers with mental health problems. All the mothers in this high-risk comparison group were recruited during pregnancy by clinicians serving as research co-workers from an outpatient clinic in Oslo (Nic Waals Institute), where women are referred to treatment for various psychiatric problems while pregnant, and one woman was also recruited from an outpatient clinic in Fredrikstad (The Children's Station¹). The women were primarily referred for treatment for depression and anxiety. Twenty-five women were recruited, but two withdrew shortly thereafter and one woman had a stillbirth, hence leaving 22 mothers and infants from this group participating in the study. No use of illicit substances was reported among the women in this group, although one woman (4.8%) reported a use of benzodiazepines during the 1st and 2nd trimester. One woman (4.8%) reported a weekly use of alcohol in the 1st trimester, six (28.6%) reported daily smoking in the 1st trimester, five (23.8%) in the 2nd trimester, while three (14.3%) reported daily smoking in the 3rd trimester.

Participants in a low-risk comparison group ($n=30$) were recruited by midwives from child health centers in Oslo. These are free-of-charge clinics where almost all expectant mothers go for regular follow-ups during pregnancy, and where the parents come with their children from infancy to age 4 for regular health and developmental check-ups and vaccinations. The inclusion criterion for the third group was being pregnant and having no known substance abuse or mental health problems. None of the 30 women in the comparison group reported the use of illicit substances during their pregnancies. Two (6.7%) reported daily smoking in the 1st trimester and one (3.3%) reported daily smoking in the 2nd and 3rd trimester. Three women (10%) reported a weekly use of alcohol in the 1st trimester, whereas none reported any weekly use of alcohol in the 2nd or 3rd trimesters. Eighteen (60%) women in this group reported a monthly intake of alcohol in the 1st trimester, seven (23.3%) reported an infrequent use in the 2nd trimester and one (3.3%) reported an infrequent use during the 3rd trimester.

The study group, along with the high- and low-risk comparison groups, were enrolled in the study during pregnancy from December 2004 to January 2009. In addition, an earlier time cohort consisting of mothers and their infants born in 1991-1996, comprised of a group

¹ In Paper I, The Children's Station in Fredrikstad was mistakenly listed as one of the residential treatment institutions for substance abuse problems. This error has no implications for the findings.

of mothers with substance abuse problems ($n=78$) and a low-risk comparison group ($n=58$), also served as comparison (Paper I). The mothers in the study group were dependent on poly-substances, although mainly opioids. They were recruited after pregnancy from the Aline Infant and Family Center, a social service institution for families with children from 0-2 years situated in Oslo. The mothers in the comparison group in this cohort were recruited from child health centers in Oslo, and none of the 58 women in this group reported the use of any substances during their pregnancies. Eight (13.8%) reported sporadic smoking, though none reported alcohol use during their pregnancies. No standardized instrument was applied to register the report of alcohol during pregnancy for this group, so one can assume that the use of alcohol in this group was underreported.

All of the participants in the study were of Norwegian ethnicity.

3.2 The present sample

The number of eligible participants varied across the three papers depending on the relevant research questions.

In Paper I, the inclusion criteria for the study group was that they had undergone detoxification while in residential treatment. Therefore, only the mothers with an ongoing substance abuse while pregnant and their infants were included from the study group in the analyses. Five (16.1%) of the 31 mothers who reported not having used substances while being pregnant, but who were admitted to treatment due to a history of substance abuse and fear of relapse, were excluded from the analyses. One mother reported not having used substances while pregnant, but the infant produced a positive meconium test and was therefore included in the analyses. In addition, five (16.1%) mothers in the study group were excluded from the analyses due to missing data on background variables. There was one fraternal twin pregnancy in the study group; consequently, a total of 21 mothers and 22 infants (12 boys) from the study group were included in the analyses. All mothers and infants from the concurrent low-risk comparison group ($n=30$, 18 boys) were included, together with the two groups from the earlier time cohort, the risk group ($n=78$, 45 boys) and the comparison group ($n=58$, 35 boys).

In Paper II, four children from the study group had been foster placed. Because the mother-infant interaction was one of the areas of interest, the children in foster placement were excluded from the analyses. Clinicians at the treatment institutions who had closely followed the mothers and infants served as research co-workers and performed the assessments for nine of the children at the age of 2 years. These assessments were excluded

from the analyses in order to avoid potential bias in the results. In order to ensure objectivity, only the children who were assessed by psychologists with no relationship to the child or mother were included. There were two fraternal twins in the study group; hence, in Paper II, 18 mothers and 20 infants (11 boys) from the study group, 22 (8 boys) from the high-risk comparison group and 30 infants (18 boys) from the low-risk comparison group were included in the analyses.

In Paper III, the inclusion criterion was participation at the 4½-year follow-up. At this time point, there had been some attrition. One fraternal twin pair remained in the study group, in which 21 mothers/caregivers and 22 children (11 boys) participated. Eighteen mothers/children (7 boys) from the high-risk comparison group participated, while 26 mothers/children (16 boys) from the low-risk comparison group participated in the follow-up and were all included in the analyses.

3.3 Ethical Considerations

Approval was granted from The Norwegian Data Inspectorate and the Norwegian Social Science Data Services for the investigation of the earlier time cohort. The project was conducted in accordance with the Declaration of Helsinki. For the investigation of the three groups recruited from 2004-2009, approval was granted by the Norwegian Regional Committee for Medical Ethics in the Eastern Health Region and by the Norwegian Social Science Data Services.


In both cohorts, all caregivers gave their informed consent and they were informed about the aims of the study. For the three groups recruited from 2004-2009, the mothers/caregivers signed an agreement of participation during pregnancy and again at child age of 2 and 4½ years. It was made clear both verbally and in writing that they had the possibility to withdraw from the project at any time. Since children are not able to give informed consent to participate in research, it is of pivotal importance to ensure that their interests are protected. In the cases where the children had been foster placed, The Norwegian CPS would consider whether it was advisable for the child to participate in the assessment, and they would further give permission to the foster parents to sign the participation agreement. All participants were encouraged to ask questions and raise potential concerns, and care was taken to ensure that the participating children were informed about the study in an age-appropriate manner, as well as the methods used at the various time points during the project. All children received a small gift such as a toy or a book for their participation. At the testing at age 2 and 4½ years, the test situations were designed to support the child in

accomplishing the tasks within a reasonable time limit, as the time spent and breaks needed during the testing varied depending on each child's needs. The primary caregiver, either the birthmother, father or foster parent, accompanied the child at all times, and was seated in the same room as the child during the test situation at the 2 and 4½ years-assessments.

3.4 Materials and Measures

The measures used from pregnancy until child age 4½ years are depicted in Figure 1, and are thoroughly described below in the order of the time points applied.

Figure 1 Measures from pregnancy until 4½ years of age



Pregnancy	Birth	3 months	12 months	2 years	4½ years
EuropASI and additional questionnaire: Substance use, alcohol use, cigarette smoking, demographic data	Medical birth records: Birth weight, head circumference, gestational age, NAS	EPDS: Postnatal Depression	PCERA: Maternal intrusiveness and lack of sensitivity in interaction	MSEL: Expressive and Receptive Language Skills	WPPSI-III : Cognitive functioning CBCL/TRF: social-emotional functioning
MCMI-III: Borderline and antisocial personality traits	Meconium samples				SCL-25: caregiver symptoms of anxiety and depression
					Semi-structured interview: Demographic data

3.4.1 Measures during pregnancy (Papers I, II and III)

3.4.1.1 Substance use

All mothers recruited from 2004-2009 were interviewed by trained researchers during pregnancy using the *European Addiction Severity Index* questionnaire (EuropASI), fifth edition (McLellan et al., 1992). The EuropASI consists of numerous questions related to different areas of functioning, such as physical health, education, work and income, alcohol,

illegal substances and medication, criminal offenses, family and social relationships and psychiatric condition. The reliability and validity of this instrument has been reported to be satisfactory (Carise, McLellan, Gifford, & Kleber, 1999; Kokkevi, Stefanis, Anastasopoulou, & Kostogianni, 1998; McLellan et al., 1992). The EuropASI was translated into Norwegian and then back translated (Lauritzen & Nøklebye, 2010), and the back translation was accepted by the Amsterdam Institute for Addiction Research.

A structured interview providing a more thorough assessment of the use of substances, nicotine and alcohol during pregnancy, was designed for the purpose of the study. This questionnaire consisted of items related to the pregnancy and residential treatment, as well as questions about how frequently illegal substances and nicotine were used, and the frequency of alcohol consumption before and during pregnancy.

Data on substance use and the social background of the women with substance abuse problems in the earlier time cohort (recruited from 1992-1996) was collected from the women's medical and social records and from verbal self-reports given to nurses working in a perinatal risk project team at Ullevål Municipal Hospital in Oslo, where the women were enrolled during their pregnancies. Due to many of these women's heavy substance abuse, the fact that they were outpatients, were using poly-substances and that some were enrolled in the risk project late in their third trimester, it was difficult to obtain reliable accounts of the amount, timing, frequency and duration of drug abuse. Heroin was reported as the main drug of choice for 53% of the women and all the women used poly-substances (Moe, 2002; Moe & Slinning, 2001; Slinning, 2004). All of the 78 women reported smoking tobacco on a daily basis throughout their pregnancies, and 24.4% of the women reported some use of alcohol during their pregnancies. In general, poor functioning and heavy long-term substance abuse characterized this group (for more background information, see Moe and Slinning, 2001).

3.4.1.2 Maternal mental health and personality traits

Millon's Clinical Multiaxial Inventory-III (MCMI-III) is a self-report questionnaire used to assess the presence of psychiatric problems. The MCMI-III comprises 175 common statements about attitudes and feelings, with each statement scored as true or false, and the scores yielding measures on five scales: clinical personality patterns, severe personality pathology, clinical syndromes, severe clinical syndromes and modifying indexes. MCMI-III was developed to correspond with the diagnostic criteria and categories of the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) (American Psychiatric Association & Association, 1994). The internal consistency of the clinical scales ranges from =.66 to .90

(Cronbach's alpha), but exceeds .80 for 20 of the subscales (Millon, Millon, Davis, & Grossman, 1997). The forms were scored with a database program called Q – Local. In the present study, the antisocial- and borderline trait subscales were used. There are 17 items assessing antisocial traits, with these items reflecting irresponsibility, failure to conform to social norms, deceitfulness and lack of remorse, impulsivity and irritability and aggressiveness. The internal consistency of the antisocial subscale is .77 (Millon et al., 1997). Sixteen items assess borderline traits, which reflect a pattern of unstable and intense relationships, fear of abandonment, feelings of emptiness, affective instability, intense anger or difficulty in controlling anger, as well as unstable self-image and sense of self. The internal consistency of the borderline subscale is .85 (Millon et al., 1997). For each of the subscales, a score of 75 or greater is considered clinically significant, whereas the occurrence of items within each scale scored as true yield information about the presence of a trait. In the present study, we did not attempt to form a personality profile or diagnosis, but simply used the subscales as indicators of the possible presence of personality traits.

3.4.2. Measures at birth (Papers I and III)

3.4.2.1 Neonatal data

Information about birth weight, gestational age, head circumference and Neonatal Abstinence Syndrome (NAS) were obtained from each child's medical record at the hospitals where their mothers gave birth. NAS was assessed by trained nurses using the Finnegan score (Finnegan, Connaughton, Kron, & Emich, 1975) with a cut-off score at ≥ 8 classifying for NAS.

3.4.2.2 Meconium samples

For the study group, meconium samples were gathered in order to investigate with greater certainty the different types of substances the children were exposed to in utero. Meconium is the first stool passed by the infant after birth and can detect substance use throughout the second half of pregnancy (Lester et al., 2001). After a demonstration and instruction by nurses at the hospital, the mothers were asked to collect the first meconium from their infants after birth. These samples were analyzed at St. Olav's Hospital in Trondheim, Norway. Meconium samples were successfully gathered for 16 of 31 women in the study group.

3.4.3 Measures at infant age of 3 months (Paper II)

One of the aims of Paper II was to investigate the association between maternal postnatal depression and child language functioning. Maternal postnatal depression was assessed at infant age of 3 months using the Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden,

& Sagovsky, 1987). EPDS is a well-validated and widely used method especially designed to screen postnatal depression (Cox, Chapman, Murray, & Jones, 1996). It consists of ten items concerning depressive signs experienced during the past seven days. Each statement is rated on a four-point scale from 0 to 3, and a higher total score indicates the presence of more symptoms. A score above 12 points (cut-off > 12) indicates a risk for clinical depression.

3.4.4 Measures at 12 months (Paper II)

At 12 months, a semi-structured play situation was administered and video recorded. The mothers were instructed to play as usual with their infants for 15 minutes with a given set of age-appropriate toys in a consecutive order. Seven minutes of the play situation where the mothers and their infants were playing with a toy kitchen, were coded and scored applying the Parent-Child Early Relational Assessment (PCERA) (Clark, 1999). The PCERA is a video-based parent-child assessment method that consists of 65 items that may be clustered into three parental (henceforth maternal), two child and two dyadic subscales. The discriminative validity of PCERA has been established by demonstrating differences between dyads in high-risk and non-risk groups (Clark, 1999, 2006). All items in the PCERA were rated on a 5-point Likert scale, with scores 1 and 2 describing an area of concern, a score of 3 describing an area of some concern and scores 4 and 5 describing an area of strength. One of the aims of Paper II was to investigate whether maternal intrusiveness and insensitivity in mother-infant interaction could be a mediating factor linking maternal psychiatric symptoms and child language functioning. Therefore, it was decided to use the subscale “maternal intrusiveness and lack of sensitivity” from the manual. This subscale includes the mother’s intrusiveness, inconsistency and unpredictability in addition to lack of structuring or facilitating the interaction. It also rates the mother’s amount of verbalization, her anxious mood and the quality and amount of physical contact in the interaction. Maternal insensitivity and unresponsiveness to the child’s cues, as well as rigidity are also assessed on this subscale. Two coders who were trained and highly experienced in coding PCERA performed the scoring of the interaction pattern. They were blind to participant group allocation and were not acquainted with the participants. In order to evaluate coder agreement, 20% of the video recordings were randomly selected and coded by the two independent scorers.

3.4.5 Measures at 2 years (Paper II)

Child language skills were examined using the Mullen Scales of Early Learning (MSEL) (Mullen, 1995), that was administered by two independent trained psychologists. MSEL is

designed for infants/children from 1 to 68 months of age. In addition to Receptive (33 items) and Expressive language (28 items), the MSEL comprises Gross Motor-, Visual Reception- and Fine Motor development. The Receptive language scale includes items such as a child's ability to listen to verbal input, comprehend questions and follow directions. The Expressive scale includes measures of auditory memory and comprehension, as well as spontaneous language and abstract reasoning. Each subscale yields raw scores and T-scores ($M=50$; $SD=10$), percentile ranks, age equivalents, and a descriptive category (e.g. above average, average, below average). T-scores below 30 are seen as an indication of a significant developmental delay. The reliability and validity of these scales have been found to be satisfactory. Norwegian norms for MSEL were not available at the time point of testing so US norms were applied. Due to a slight variability in age at the time point of the testing, T-scores were used in the statistical analyses instead of raw scores.

3.4.6 Measures at 4½ years (Paper III)

3.4.6.1 Child cognitive functioning

In order to assess key aspects of cognitive functioning, the Norwegian edition of the Wechsler Preschool and Primary Scale of Intelligence, third edition (WPPSI-III) (Wechsler, 2008) was administered. WPPSI-III (Age 2:6 to 7:3) is constructed of 14 subtests measuring verbal and logical/problem-solving skills, as well as tasks capturing speed and receptive language. WPPSI-III yields a verbal IQ and a performance IQ as well as sum scores of speed and receptive language, all with expected means of 100 and expected standard deviations of 15 based on Norwegian norms. The full-scale IQ is calculated based on seven of the subscales, and was obtained for all 66 children from the three groups who participated at the 4 ½-year follow-up.

3.4.6.2 Child social-emotional functioning

To assess child social-emotional problems two versions of the Achenbach System of Empirically Based Assessment (ASEBA) were used, the Child Behavior Check List (CBCL) 1 ½ -5 and the Teachers Report Form (TRF) (Achenbach & Rescorla, 2000). These questionnaires are well-validated, standardized assessment protocols for child behavior problems designed for completion by primary caregivers and teachers. Norwegian norms for the ASEBA were not available at the time point of testing, thus US norms were applied. The ASEBA has been translated into Norwegian and then back translated with the permission of

T.M. Achenbach². Each mother/caregiver was asked to fill out the form in prior to the 4½ year follow-up assessment. Granting mother/caregiver consent, following the 4½ year examination the TRF was sent to the child's preschool accompanied by a letter. The preschool teacher with the closest relationship to the child was asked to fill out the form and return it by mail.

The CBCL and TRF each consist of 99 items where every item is to be answered on a three-point scale from 0 to 2, where 0 is "not true", 1 is "somewhat true" and 2 is "often true". The items constitute eight factors of emotional, behavioral and social problems, and can also be categorized into internalized and externalized behaviors, in addition to a total behavior problem score. Internalized behaviors include items from the four dimensions of *emotionally reactive*, *anxious/depressed*, *withdrawn* and *somatic complaints*. Externalized behaviors include items from the two dimensions of *attention problems* and *aggressive behavior*. The total behavior problem score also includes the dimension *sleep problems* (only in the CBCL), as well as the rest of the items described as *other problems*. A T score from 65 to 69 is considered within the borderline range, and a T score above 70 is considered within a clinical range of problems. In order to take account of the full range of variation in the scales, the sum of the raw scores was used in the present study (Achenbach & Rescorla, 2000).

3.4.6.3 Maternal/caregiver symptoms of anxiety and depression

An assessment of anxiety and depression was obtained by use of the short version of the Hopkins Symptom Checklist, SCL-25 (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974), which the mother/caregiver was asked to fill out in advance of the 4 ½-year assessment. SCL-25 is a self-administered questionnaire consisting of 25 items representative of the symptoms of anxiety and depression, where each item is rated on a five-point scale ranging from 0 (not at all) to 4 (very much). SCL-25 has been shown to have a satisfactory validity and reliability as a measure of psychological distress (Strand, Dalgard, Tambs, & Rognerud, 2003). Ten of the items are related to symptoms of anxiety and 15 to symptoms of depression.

3.4.6.4 Demographic characteristics and substance use at child age 4½ years

A semi-structured interview designed for the purpose of the study was performed to register the caregivers' current educational level and whether they were living alone or with a partner

² Translated to Norwegian by T.S. Nøvik and colleagues in 2002, and back translated by S. Schanche and T. Ueland in 2002.

or other adults. The child's living situation (living with biological parents or foster parents) was also recorded. Additionally, the mothers/caregivers were asked a set of questions regarding current problems with substance abuse, and whether they were receiving help for their substance abuse problems.

3.5 Statistical Analyses

3.5.1 Paper I: The perinatal outcome of children born to women with substance dependence detoxified in residential treatment during pregnancy

The groups from the two time cohorts were compared on the children's perinatal data; NAS, prematurity, gestational age, birth weight and head circumference. For NAS the difference between the substance-exposed groups were analyzed by exact chi-square tests for independence. Apgar scores between the substance exposure groups were compared by exact Mann-Whitney tests. For gestational age, birth weight and head circumference differences between combinations of cohort and substance exposure groups were analyzed by linear regression, with an interaction between treatment and cohort to investigate whether differences between substance exposed and non-exposed children were the same in the two cohorts. The regression analyses were repeated with gender as an additional covariate, and with the twins excluded. Effect sizes for two-group comparisons were based on differences between group means with pooled standard deviations based on actual data and group sizes, expressed as Cohen's d , i.e. the difference between two means divided by a standard deviation for the data.

3.5.2 Paper II: Mother–Child Interaction and Early Language Skills in Children Born to Mothers with Substance Abuse and Psychiatric Problems

The three groups were compared on maternal age and education, using ANOVA. For single parenthood and categories of maternal education level, group differences were analyzed by exact chi-square tests. ANOVA was also conducted to test the differences between groups on the dependent variables (Receptive and Expressive Language from the Mullen Scales of Early Learning), and as secondary analyses on group differences on the independent variables (antisocial and borderline personality traits as well as postnatal depression). Post-hoc Tukey Honestly Significant Difference (HSD) tests were performed to examine the statistical significance of differences between pairs of groups in the ANOVA analyses. Linear regression analyses were performed to investigate whether observed group effects were dependent on adjustment for socio-demographic factors (maternal age, education and single parenthood).

Internal consistency of the scales for postnatal depression and maternal intrusiveness in interaction, were reported as Cronbach's alpha.

A dichotomous variable capturing substance abuse during pregnancy or not was computed and named "substance exposure", to be used in the regression analyses. This variable was based on items from the interview designed for the purpose of the current study covering the use of various substances during pregnancy.

In order to investigate to what extent prenatal substance exposure, maternal antisocial and borderline personality traits, postnatal depression at 3 months and maternal intrusiveness in social interaction observed at 12 months predicted expressive and receptive language skills at 2 years, two linear hierarchical regression analyses were performed with Receptive and Expressive Language at 2 years, respectively, as dependent variables. These included the following independent variables: Substance exposure at Step 1, antisocial personality traits, borderline personality traits and postnatal depression added at Step 2, and maternal intrusiveness observed in interaction between mother and child added at Step 3. To investigate to what extent such relationships could be observed independently of single parenthood and maternal education, these demographic variables were included at Step 4 in the hierarchical regression analyses.

Power calculations were based on the model in step 4 with seven independent variables, an anticipated R square of 0.20, and 80% power.

Lastly, three separate mediation analyses with maternal psychiatric symptoms as predictors (maternal antisocial traits, maternal borderline traits and postnatal depression), maternal intrusiveness in the mother-child interaction as a mediator and child language skills as an outcome variable were performed. Mediation analyses were performed using conditional process analysis (Hayes, 2013; Preacher & Hayes, 2008) with 10,000 bootstrap samples, and bootstrap bias corrected 95% confidence intervals were computed for the mediated effects. Indirect effects were considered significant if bias-corrected confidence intervals did not contain zero (Hayes, 2013). The analyses were rerun with the covariates maternal age, education, and single parenthood.

3.5.3 Paper III: Cognitive and Social-emotional Functioning at 4½ Years in Children Born to Mothers who have Received Treatment for Substance Abuse Problems while Pregnant

Descriptive statistics were applied to investigate the sample characteristics of substance use during pregnancy with the sample at the 4 ½-year investigation. Linear regressions with group as independent variable and gender as covariate were conducted to test the differences

between groups in birth weight and on WPPSI-III (where standardized scores are according to age). Linear regression analyses with group as independent variable, and gender and test age as covariates were conducted to test for group differences in CBCL and TRF raw scores. Furthermore, sensitivity analyses excluding the twins were performed for child birth weight. For birth weight, WPPSI-III, CBCL, TRF and SCL, sensitivity analyses were performed excluding the foster children/foster parents, with 95% bootstrap BC_a intervals (10,000 bootstrap replications) computed for changes when the significance of the change was not clear from considerations of overlap of confidence intervals.

One-way ANOVAs were conducted to test for differences between groups on current symptoms of caregiver anxiety and depression (SCL-25) and group differences in single parenting. For SCL-25, sensitivity analyses were performed excluding the foster parents.

Exact chi-square tests were conducted to investigate group differences in caregiver education at 4½ years. Post-hoc Tukey Honestly Significant Difference (HSD) tests were performed to examine the differences between pairs of groups in the ANOVA analyses, and in the linear regression analyses with adjustment for gender only. In the linear regression analyses with adjustment for age and gender as well as in the chi square analyses, it was corrected for multiple testing by the Holm procedure (Aickin & Gensler, 1996).

In order to investigate whether group differences at age 4½ years could be mediated by birth weight, mediation analyses were run for the outcome variables (cognitive and social-emotional functioning at 4½ years) with birth weight as a possible mediator of group. Furthermore, to investigate whether birth weight could mediate group differences independently of social risk factors, such as single parenthood, low caregiver education and caregiver mental health problems measured at 4½ years, mediation analyses were also performed adjusting for these variables. A dichotomous variable capturing higher/lower caregiver education was computed and used in these analyses. Mediation analyses were performed using conditional process analysis (Hayes, 2013; Preacher & Hayes, 2008) with 10,000 bootstrap samples, and bootstrap bias corrected 95% confidence intervals were computed for the mediated effects.

3.5.4 Statistical considerations

All analyses were performed using a significance level of 0.05 (two-tailed).

3.5.4.1 Missing data

In Paper I, where there were missing values on the dependent variables, the cases were excluded from the analyses. In Paper II, there were some missing values in the independent variables. The hierarchical regression analyses were therefore performed using multiple imputation with 200 imputed datasets (Carpenter & Kenward, 2012) to handle missing values in the independent variables, while three cases with missing values on the dependent variables were excluded. The imputation model included expressive and receptive language and all covariates in Step 4. In Paper III, the inclusion criteria for the study was participation at the 4 ½-year follow-up, therefore there were no missing values on the WPPSI-III. Where there were missing cases on CBCL and TRF, these were excluded from the analyses. On SCL-25 there were four missing cases. To handle this, scale scores were computed as means of valid items multiplied by the total number of items, if at least half of the items within each scale were valid.

3.5.4.2 Causality

The design in the present study was non-experimental; for this reason, no conclusions about causality can be drawn. Although adjusting for other possible causal factors in the analyses, the possibility of other unidentified factors causing the observed relationships cannot be excluded with the present design.

3.5.4.3 Small sample sizes, statistical power and Type II error

With small sample sizes such as the present one, the number of covariates entered into the analyses and models is limited. Consequently, controlling for or demonstrating possible relationships with other variables was not always possible, nor was investigating more complex models of moderating factors. Hence, both theoretical and pragmatic considerations were made before conducting the data analyses. Controlling for child age was not possible in the analyses in Paper II due to the limited sample size. Therefore, it was decided to use T-scores in the regression analyses, although it is usually recommended to use raw scores. Moreover, statistically significant effects and group differences are more difficult to detect in smaller samples, which increases the likelihood of not rejecting a false null hypothesis (committing a Type II error). Doing research on clinical groups often implies small samples. Because clinically significant findings may be statistically insignificant, it is important to be careful not to conclude or generalize from statistically insignificant findings particularly with small sample sizes.

3.5.5 Statistical software

All analyses were conducted using SPSS (versions 18/19/20) or R (The R Foundation for Statistical Computing, Vienna, Austria) whereas SPSS with the PROCESS routine (Hayes, 2013) was used for conditional process analysis. R was used for multiple imputation with the package mice, for Holm adjustment with the R function p.adjust and for bootstrapping using the R package boot. For power calculations, R was used with MBESS (function ss.power.R2).

4 SUMMARIES OF PAPERS

4.1 Paper I: The perinatal outcome of children born to women with substance dependence detoxified in residential treatment during pregnancy

Aims

The study aimed to investigate the perinatal outcome of children born to mothers with opioid- and poly-substance abuse problems who underwent detoxification in residential treatment institutions during pregnancy compared to infants born to women with substance abuse problems at a time when no such treatment was available.

Methods

Information about infant birth weight, head circumference, gestational age and Neonatal Abstinence Syndrome (NAS) was gathered from the infants' birth journals in both cohorts. The perinatal data of the infants born to mothers detoxified in a residential setting during pregnancy (n=22) was compared to the data on infants born to mothers receiving no treatment (n=78). Both study groups had concurrent comparison groups (n=30, n=58).

Main results

Linear regression analyses showed significantly better perinatal outcomes on gestational age and head circumference, and a close to significantly higher birth weight for the infants born to mothers who underwent detoxification while pregnant, as compared to the infants from the earlier time cohort whose mothers did not receive residential treatment. None of the infants born to mothers detoxified showed any symptoms of NAS compared to 77% in the earlier cohort, and none of the infants were born prematurely as compared to 25.6% of the infants in the earlier cohort. The difference in gestational age and head circumference between the infants exposed to substances and their respective comparisons was significantly higher in the earlier cohort where the mothers had not received help than in the cohort where the mothers were detoxified. However, this was not found for birth weight, although it was close to statistical significance. There were no miscarriages, complications or morbidities associated

with residential detoxification treatment, nor did any of the women who were voluntarily institutionalized drop out from the treatment or relapse into drug abuse while in residential care.

4.2 Paper II: Mother–Child Interaction and Early Language Skills in Children Born to Mothers with Substance Abuse and Psychiatric Problems

Aims

This study aimed to investigate how maternal antisocial- and borderline personality traits and postnatal depression, substance abuse and maternal intrusiveness in interaction were related to early child language skills.

Methods

Three groups of mothers were recruited during pregnancy: One from residential treatment institutions for substance abuse ($n=18$), one from psychiatric outpatient treatment ($n=22$) and one from child health centers ($n=30$). Maternal substance use and antisocial- and borderline personality traits were assessed during pregnancy, postnatal depression at infant age 3 months, maternal intrusiveness in interaction at 12 months, and child language skills at child age of 2 years.

Main results

Mothers with a history of substance abuse problems had the lowest level of education, they were younger and they were more likely to be single mothers than the mothers in the two other groups. The children born to mothers with substance abuse problems scored significantly lower on expressive language functioning than the children born to the low-risk comparison mothers, though not when controlling for maternal age, education and single parenthood. Higher levels of maternal intrusiveness in interaction at 12 months were observed within the study group than the two comparison groups, however not when controlling for the mentioned socio-demographic risk factors. No significant group differences in receptive language skills were detected. In a hierarchical regression analysis with substance exposure, antisocial- and borderline personality traits, postnatal depression and maternal intrusiveness with expressive language as dependent variable, only maternal intrusive behavior exerted a unique significant relationship with expressive language at 2 years, also when controlling for socio-demographic risk factors.

4.3 Paper III: Cognitive and Social-emotional Functioning at 4½ Years in Children Born to Mothers who have Received Treatment for Substance Abuse Problems while Pregnant

Aims

This study aimed to examine child cognitive and social-emotional functioning at 4½ years of age in children born to mothers recruited from residential treatment institutions for substance abuse where they received help while pregnant (n=21), in comparison to a high-risk and a low-risk group of children. The high-risk group comprised children born to mothers with mental health problems recruited from psychiatric outpatient treatment while pregnant (n=18), and the low-risk group comprised children born to mothers with no such problems who were recruited from child health centers while pregnant (n=26). Furthermore, the study aimed to investigate whether child birth weight could mediate the possible group differences in cognitive and social-emotional functioning at 4½ years, also when adjusting for caregiver characteristics/possible risk factors such as single parenthood, low education and caregivers' mental health problems.

Methods

Birth weight was obtained from each child's medical record at the hospitals where the mothers gave birth. Cognitive and social-emotional functioning at child age 4½ years were assessed using the Wechsler Preschool and Primary Scale of Intelligence, third edition, and the Child Behavior Check List, respectively. Symptoms of caregiver anxiety and depression were assessed by SCL-25.

Main results

The mothers with a history of substance abuse were more likely to be single mothers compared to the two other groups. None of the mothers in the study group reported current problems with substance abuse, but three mothers at the 4½-year assessment were in Opioid Maintenance Treatment at this time point. No significant group differences in child cognitive functioning were found, but caregiver-rated internalizing and total social-emotional problems were significantly higher in the children born to mothers with substance abuse problems compared to the low-risk comparison group and similar to that of the high-risk comparison group. Birth weight was found to have an effect on internalizing problems at 4½ years, and partly mediated the relationship between group and social-emotional problems, though not when controlling for caregiver socio-demographic risk factors such as low education, single parenthood and current caregiver symptoms of anxiety and depression. Caregiver anxiety and depression was also related to caregiver reports of child internalizing problems. In sensitivity analyses, when excluding seven children who were in foster care, the difference in the

caregiver report of child internalizing behavior problems between the children born to mothers with substance abuse problems and the low-risk comparison children was significantly reduced.

5 DISCUSSION

5.1 Summary of main results

Several findings emerge from the present study of children born to mothers who received help for their substance abuse problems during pregnancy.

1. *Maternal characteristics and mental health problems* (Papers I, II and III): The majority of the mothers in residential treatment for substance abuse problems were poly-substance abusers. All of the mothers using substances while pregnant were detoxified during pregnancy. Pregnancy data showed that the mothers in this group were younger, they had lower educational level and were more likely to be single parenting compared to the two concurrent groups of mothers. At child age of 4½ years, they were still more likely to be single mothers compared to the two other groups. The mothers with substance abuse problems scored higher on antisocial personality traits, and also on observer-rated intrusiveness and lack of sensitivity in interaction with their child at 12 months, than both the two concurrent comparison groups, however not when controlling for maternal age, education and single parenthood.

2. *Infant perinatal outcome* (Paper I): Compared to the infants in the earlier cohort whose mothers did not receive residential treatment, the infants exhibited significantly better perinatal outcomes on gestational age and head circumference, and none was born with NAS. Furthermore, no miscarriages, complications or morbidities were associated with residential detoxification treatment.

3. *Group differences and predictors of language skills at age 2* (Paper II): The children born to mothers with substance abuse problems scored significantly lower on expressive language at 2 years of age than the low-risk comparison children, however not when controlling for maternal age, education and single parenthood. No significant group differences in receptive language skills were detected. Maternal intrusiveness observed in mother-child interaction at 12 months was significantly related to child expressive language skills at 2 years, also when controlling for socio-demographic risk factors.

4. *Cognitive and social-emotional functioning at age 4½* (Paper III): No significant group differences in cognitive functioning at 4½ years were detected. However, with respect to social-emotional functioning, the children born to mothers with substance dependence

problems showed, albeit mostly below clinical threshold, significantly more internalizing and total problems than the low-risk comparison children and similar to that of children born to mothers with mental health problems as rated by their caregivers. Caregiver's present symptoms of anxiety and depression were related to child total score on social-emotional problems. Furthermore, birth weight was significantly related to internalizing problems at 4½ years, and partly mediated the relationship between group and internalizing as well as total score on social-emotional problems, but not when controlling for caregiver socio-demographic risk factors such as low education, single parenthood and current caregiver symptoms of anxiety and depression.

5. Foster placements by the age of 4½ years (Paper III): By the age of 4 ½, seven children born to mothers with substance abuse problems had been foster placed. Two of these children were placed in foster care before the age of 3 months while the other five were placed later and two as late as between 2–4½ years. In the sensitivity analyses, when excluding the foster children from the analyses of group differences in birth weight, the difference between the children in the study group and the low-risk comparison children was reduced, and this reduction was statistically significant. When excluding the foster children from the analyses of group differences in social-emotional problems at 4½ years, similar results were observed; the difference in caregiver report of child internalizing behavior problems between the children born to mothers with substance abuse problems and the low-risk comparison children was significantly reduced.

5.2 Interpretation and discussion of the findings

5.2.1 Maternal characteristics and mental health problems

Of the 31 mothers with substance abuse problems, six of the mothers reported not having used substances while being pregnant, but were in residential treatment for other reasons, being that their partners were currently abusing substances or that they themselves had a history of substance abuse and feared relapse. The women using substances before being admitted to the institutions were all detoxified as part of the residential treatment, though at various time points depending on when they were admitted. The mothers received medical support and guidance, as well as better nutritional and living conditions while in residential care. Moreover, none of the mothers dropped out or relapsed into substance abuse while being detoxified, and all the mothers stayed in residential care until giving birth. These findings suggest that residential care with controlled detoxification and psychosocial support can build

or strengthen the motivation for expectant mothers to become drug free. It is important to recognize that the detoxification in this study took place in a residential setting that was maintained throughout pregnancy, and in particularly controlled and supportive environments. It is likely that this close monitoring and individually adapted treatment can account for the success in detoxification. Psychotherapy, social training and a focus on the unborn child, not to mention working with prenatal attachment and psychological mother- and parenthood, were all important components in residential treatment in addition to the detoxification. The mothers in residential care also attended more of the maternity check-ups than the mothers in the earlier time cohort did. While in residential care the mothers were encouraged to take responsibility for their situation, and it is possible that the social training and support played an important role in motivating these women to attend their regular maternity check-ups. The mothers who received treatment were less likely to be single mothers than the mothers in the earlier time cohort, although they were more likely to be single mothers than the two concurrent comparison groups. At the 4½-year assessment, none of the mothers in the study group reported current problems with substance abuse, but because three mothers in this group were in Opioid Maintenance Treatment at this time point, they reported receiving treatment for substance abuse problems. In addition, one mother reported receiving help for recurring thoughts and craving for substances.

As we had expected based on previous literature, the mothers in the substance abuse group had the lowest level of education, and they were more likely to be single mothers than the mothers in the two concurrent comparison groups. As anticipated, there was also an overlap between substance abuse problems and psychiatric symptoms, with antisocial personality traits being more predominant among the mothers with substance abuse problems compared to the other two groups of mothers. Among the mothers with substance abuse problems, 30.8% scored within the clinical range on antisocial symptoms. This is consistent with findings from other studies reporting on the comorbidity between substance abuse and symptoms of antisocial personality, as well as antisocial personality disorder (Beckwith, Howard, Espinosa, & Tyler, 1999; Espinosa et al., 2001; Verheul, 2001). When controlling for maternal age, education and single parenthood, the group difference was no longer significant for antisocial personality traits. Single parenthood was then the only of the characteristics significantly related to antisocial traits and these were highly correlated. This can be understood in terms of the very characteristics of antisocial personality functioning, as it often has negative consequences for interpersonal functioning. Recent literature suggests that women with antisocial personality traits use more relational- than physical aggression

compared to men and that they are more emotionally unstable (Kreis & Cooke, 2011). According to Millon (1997), people with antisocial personality traits expect pain and rejection from others, and based on early experiences they often have inner representations of other people as being disloyal and unreliable. To encounter this expectation of others' hostile motives, they may act in an irresponsible and insensitive manner to avoid victimization and abuse.

The mothers in the study group had significantly higher levels of borderline personality traits compared to the low-risk mothers (however, not within clinical range), but similar to that of the high-risk comparison mothers, also when controlling for socio-demographic risk factors. The mothers in the study group did not score significantly higher on self-reported postnatal depression than the low-risk mothers, and scored significantly lower than the high-risk comparison mothers.

Upon the child reaching the age of 4½, we measured the presence of current caregiver symptoms of anxiety and depression and found no significant differences between the study group and the low-risk comparison mothers. However, at this time point seven (31.8%) of the children from the study group who participated in the 4½-year follow-up were in foster care. We therefore looked at whether there would be an increase in reported symptoms when we removed the foster parents from the analysis, and this was confirmed. Even so, there was still no statistically significant difference between the study group and the low-risk comparison group, thereby indicating relatively low levels of symptoms of anxiety and depression. The mothers with substance abuse problems received further help and guidance from the treatment institutions after the children were born. In addition, the Norwegian welfare system financially supports disadvantaged families through the Child Protection Service (CPS). Both the help from the treatment institutions and the financial support may have played a part in preventing these mothers from developing anxiety and depression. Nonetheless, the possibility of the under-reporting of symptoms cannot be ruled out.

In addition, from the time of recruitment and up until the children were 4½ years, there was attrition. In addition to seven biological mothers from the study group not taking part in the study anymore, because their children had been foster placed, 18 of the original 83 recruited mothers did not take part in the 4½-year follow-up, either due to uncertain whereabouts or to withdrawal from further participation in the research project. It cannot be ruled out that if all the original mothers recruited to the study were taking part in the 4½ year investigation, there would have been higher levels of symptoms of anxiety and depression,

and that it was the most highly functioning mothers that remained in the study at 4½ years. Therefore, problems with attrition may have created a bias in the study.

5.2.2 Infant perinatal outcome

In comparison to the infants in the earlier cohort whose mothers did not receive residential treatment, the infants born to mothers detoxified in residential treatment institutions showed better perinatal outcomes on gestational age and head circumference, as well as no NAS. Moreover, no miscarriages, complications or morbidities were associated with residential detoxification treatment. Children born to the mothers in residential treatment experienced less prenatal substance exposure than the children in the earlier cohort, and they seem to be born with less biomedical vulnerability. Although this study cannot isolate the effects of detoxification on perinatal outcome, the results suggest that the multi-treatment approach of the residential institutions on the whole can account for the differences in perinatal outcome between the infants prenatally exposed to substances in the earlier and later time cohort.

Although gestational age and head circumference were higher, the results show that the difference in birth weight between the two substance-exposed groups was only at a trend level and that the difference in birth weight between the substance-exposed infants and their respective low-risk comparison groups did not differ significantly between the cohorts. A lower birth weight can be a marker for a variety of other adverse prenatal environmental conditions than maternal substance abuse such as maternal cigarette smoking and under- or malnutrition in addition to psychological stress during pregnancy (England et al., 2001; Glover, 2014; Hedegaard et al., 1993; Secker-Walker et al., 1998). Thus, one explanation for the lack of a catch-up effect in birth weight may be that the majority of the women with substance dependence problems in both time cohorts were smoking throughout their pregnancies, although eight of the 21 women managed to cut their smoking completely while in residential care. Another explanation is the fact that nine (42%) of the women were admitted to residential treatment as late as the 3rd trimester. The prolonged opioid- and poly-drug exposure combined with nicotine exposure in these pregnancies, may account for a lack of a catch-up in birth weight. The relationship between prenatal nicotine exposure and infant birth weight was not investigated in the present study, but should probably be further addressed in future studies. While the mothers in residential care most probably had adequate nutrition during pregnancy, there was no registration of the variety in their food intake prior to the residential treatment. It is also possible that the mothers with substance abuse problems experienced psychological stress while pregnant, which may have contributed to the observed

difference in birth weight between their infants and the low-risk control infants. However, all of these infants were within the normal range of gestational age, hence suggesting that maternal psychological stress during pregnancy is probably not the primary explanatory factor for the lower birth weight.

In the sample participating at the 4½-year follow-up, there were significant differences in birth weight between the group of children born to mothers with substance abuse problems and the low-risk comparison children. This difference was reduced when the foster children were excluded from the analyses, and this reduction was statistically significant. This finding that the foster children had a lower birth weight relative to the other children in the study group may indicate a larger biomedical vulnerability for the children who were foster placed.

There was no significant difference in birth weight between the group of children born to mothers with substance abuse problems and the high-risk comparison group. It is important to underscore that there were relatively low levels of prenatal substance exposure in the group of mothers recruited from residential treatment institutions, and there were no reports of prenatal substance abuse in the high-risk comparison group. Maternal cigarette smoking during pregnancy occurred in both groups, although it was more prevalent in the group of mothers with substance abuse problems, thereby possibly exerting an influence on infant birth weight. Like the mothers in the study group, it is also likely that the mothers in the high-risk comparison group experienced psychological stress while pregnant, as they were recruited from an outpatient clinic where they were admitted for mental health problems. This kind of maternal psychological stress may have had an influence on the prenatal growth in their infants.

5.2.3 Group differences and predictors of language skills at age 2 years

No clear and significant group differences in child receptive language skills could be detected, but for expressive language, the children of mothers with substance abuse problems scored significantly lower than the low-risk comparison children and similar to that of the high-risk comparison children. It is possible that children growing up in a non-optimal caregiving environment are more delayed in the area of expressive language, rather than in the area of receptive skills. This usually suggests a normal cognitive capacity (Benedict, 1979). When controlling for single parenthood, maternal age and education, the group difference in expressive language was no longer significant. Because single parenting, lower maternal age and educational level were more present in and characterized the study group, it is possible that these maternal risk factors exceeded the effects of group belonging per se.

There was no significant relationship between prenatal substance exposure and child language skills. It is important to bear in mind that the mothers in the substance abuse group were in treatment for substance abuse problems, and that all the mothers using substances were detoxified during their pregnancies. Seven of the mothers in this sample reported that they had not used any substances while pregnant, but were under treatment for other reasons, such as earlier substance abuse problems and fear of relapse. The children in this group were therefore either not at all prenatally exposed to substances or to a lesser extent than reported in many other studies, possibly minimizing the biomedical risk for aberrant language development. However, the sample size is not large; therefore, we cannot totally rule out possible effects of the prenatal substance exposure that did occur on language development. It is possible that we would have discovered effects of prenatal substance exposure with a larger sample size.

Together with maternal intrusiveness and insensitivity in interaction, maternal antisocial personality traits were significantly related to child expressive language skills before adjusting for maternal education and single parenthood. After adjusting for these demographic variables, only maternal intrusiveness and insensitivity exerted a uniquely significant relationship with expressive language, while neither substance exposure, borderline personality traits nor postnatal depression were significantly related to child expressive language skills. When a child grows up in an unpredictable relationship with the mother, characterized by intrusiveness and lack of sensitivity, it is possible that some of the interpersonal precursors of language development are compromised, thus adversely affecting the child's developing language skills. We found that maternal intrusiveness observed in mother-child interaction at 12 months was highest in the group of mothers with substance abuse problems. One explanation for the higher levels of antisocial personality traits, as well as higher levels of maternal intrusiveness in mother-child interaction, may be that maternal antisocial traits are expressed to their children through intrusive and insensitive interactions. Maternal unpredictability and insensitivity may possibly inhibit the child from vocalizing and expressing early language. Still, to be better able to understand the complex pathways and different factors that may affect child language development, the surroundings that individuals and families live in also have to be taken into consideration. In other words, it is important to look at both the proximal factors (such as characteristics of the close interaction between the child and the mother) and the more distal factors related to the mother's psychological and social situation. It has been well documented that distal risk factors such as low socioeconomic status, single parenthood and low levels of education among parents can

put a child at multiple risk for worse developmental outcomes (Beeghly & Tronick, 1994). It could be that when a child lives alone with a mother with a history of substance abuse, there might be few corrective actions from other adults to compensate for non-optimal stimulation and possibly an unpredictable and insensitive environment. Jeremy and Bernstein (1984) examined a host of risk- and protective factors that affected mothers' interactions with their infants, and found that the total resources mothers had at their disposal predicted their interactive skills better than to what extent they had a substance abuse problem per se (Jeremy & Bernstein, 1984).

It is also possible that maternal antisocial personality traits themselves are related to other potentially causative variables. For instance, it has been shown that antisocial personality traits are related to general cognitive ability (Heinzen, Kohler, Godt, Geiger, & Huchzermeier, 2011), so it is possible that children whose mothers display such traits will possess a genetically based vulnerability for poor language development. The group differences in antisocial personality traits were reduced when controlling for maternal education level, hence suggesting a possible genetic vulnerability, yet both low maternal education and antisocial personality traits can be explained by variables other than genetic factors, such as an maternal aversive childhood history, poor relationships and own parents with substance abuse problems among others. These issues should be addressed in future studies.

In the present study, it is possible that the sum of cumulative risks factors influenced the mothers' caregiving capacities expressed in their insensitivity and intrusiveness when interacting with their infants. These risks may be distal factors in terms of low education, poor network and low income in addition to proximal factors in terms of the absence of a second supportive caregiver and the presence of maternal psychosocial challenges and psychiatric symptoms such as antisocial personality traits.

5.2.4 Cognitive and social-emotional functioning at age 4½ years

On average, the group of children born to mothers with substance abuse problems scored lower on all WPPSI subscales and on the total score than the high-risk comparison group, who in turn scored lower than the low-risk comparison children. Yet, none of these group differences were statistically significant. As discussed above, the study group in the present sample was characterized by a low level of prenatal substance exposure as the women were detoxified while pregnant, and lived under safe and stable conditions and high monitoring when in residential care. Earlier studies documenting differences in cognitive functioning

relative to controls have often been based on samples of children with higher levels of prenatal substance exposure and less supportive follow-up (Hans & Jeremy, 2001; Moe, 2002; Moe & Slinning, 2002). The families where the mothers had substance abuse problems received further help and guidance from the treatment institutions after the children were born, and some mothers and their infants remained in the treatment institutions up to one year after birth. Through the CPS the Norwegian welfare system also financially supports disadvantaged families so that the children can attend preschool, which all the children in the present study did. Taken together, all these factors may have contributed and stimulated a positive cognitive development. However, it is also possible that the WPPSI did not capture some of the more subtle problems of concentrating and attention span, which have previously been found among children prenatally exposed to opioids and other substances (Konijnenberg & Melinder, 2013; Lester & Tronick, 1994; Melinder et al., 2013).

Regarding social-emotional functioning at 4½ years, the children born to mothers with substance dependence problems had significantly more caregiver-rated internalizing problems than the children in the low-risk comparison group, and similar to that of the high-risk comparison group. The children born to mothers with substance abuse problems and the children in the high-risk comparison group also had significantly a higher total score on social-emotional problems, as well as a trend towards more caregiver-reported externalizing problems than the low-risk comparison children. It should be noted, however, that although there were significant group differences, only three children (13.6%) in the study group scored within the borderline or clinical range; this was on internalizing and total problems. On the teacher-rated problem report (TRF), we found no significant group differences, either in externalizing or internalizing behavior. The significant group differences in caregiver reported problems, but not in the reports provided by the preschool teachers, may be due to multiple factors. One possibility is that internalizing problems are more easily observable in the home environment, where there are fewer children and the parents have more experiences reading their children's subtle cues. It may also be the case that the preschool teachers overlooked internalizing problems such as anxiousness, depressed mood and withdrawal from play and social interaction. In preschool, "quiet" children may not get much attention from the preschool teachers who have many children to tend to, and they do not pose the same problems in a group of children as those with externalizing behavior. It is also likely that the children's behavior is situation-specific and varies between the preschool and home environment (Achenbach, McConaughy, & Howell, 1987), and it may be that the children actually show more problem behavior in the caregiver-child relationship because of a more

stressful home environment due to the caregivers' own psychosocial problems. It is also possible that the mothers/caregivers with higher levels of anxiety and depression had a readiness to see problem behavior in their children, and thereby rated the children as having more problems than the preschool teachers did. Maternal depression has been found to increase negative perceptions of children (Gelfand & Teti, 1990), and in another study of caregivers with substance abuse problems and their children, caregiver depressive symptoms predicted their ratings of child behavior problems independent of other risk factors such as substance exposure and negative aspects of the home environment (Warner et al., 2006). We did find that caregiver anxiety and depression were related to caregiver reports of child total social-emotional problems. This may imply that the caregivers with such symptoms had a readiness to see problems in their children; however, when using a transactional framework of interpretation, it is also likely that the child social-emotional problems and caregiver problems negatively influence one another over time. A child growing up with a mother with symptoms of anxiety and depression may also learn through social referencing from the mother that the world is an unsafe place, thus creating feelings of anxiety, leading to social inhibition and other internalizing difficulties. A significantly higher incidence of anxiety and depression was found among the mothers with mental health problems (high-risk comparisons) at the 4½-year assessment relative to the study group and the low-risk comparison mothers. Moreover, when excluding the foster-mothers from the study group, the difference in maternal symptoms of anxiety and depression between the study group and the low-risk comparison group increased, and this increase was statistically significant, hence suggesting higher levels of anxiety and depression among the biological mothers in the study group.

Birth weight was found to have an effect on internalizing problems, and partly mediated the group differences in both caregiver-rated child internalizing problems and total problems; even so, the mediating effect of birth weight was not significant when controlling for caregiver socio-demographic risk factors such as single parenthood, lower educational level and present symptoms of anxiety and depression. These findings illustrate the difficulty in separating the individual effects of various risk factors on child social-emotional functioning as these risk factors often coexist as a whole. The biomedical risk factors may interact with the risk factors in the proximal caregiving environment, thus enhancing the adverse effects over time. For example, a lower birth weight may express a possible biomedical vulnerability, which may further have an effect on a vulnerable mother's view of her infant and create worries. This may influence her and play a part in her caregiving capacities, which again may influence the child's behavior. The mothers in the two risk

groups may have a readiness to see problem behavior in their children, and maternal anxiety and depressive symptoms as well as child behavior problems may mutually influence and reinforce each other over time, as illustrated in the transactional model (Sameroff, 1990; Sameroff & Chandler, 1975).

5.2.5 Foster placements by the age of 4½ years

At the 4½-year follow-up, seven (31.8%) of the 22 children born to mothers with substance abuse problems had been foster placed. When excluding the foster children from the analyses of group differences in birth weight, the difference between the children in the study group and the low-risk comparison children was reduced, and this reduction was statistically significant, thereby indicating a larger biomedical vulnerability in the children placed in foster care. When excluding the foster children from the analyses of group differences in social-emotional problems at 4½ years, similar results were observed; the difference in child internalizing behavior problems between the study group and the low-risk comparison group was reduced, and this reduction was statistically significant. It may be that the foster children experienced higher levels of internalizing problems among the children in the study group. In all probability did the children who came to live in foster care experience an adverse caregiving environment prior to their placement. A decision by the Child Protection Service (CPS) of taking custody of a child is based on a thorough consideration in which other voluntary attempts have not been successful. Of the children who were placed in foster care, only two were placed before age 3 months while the other five were placed later and two children as late as between 2–4½ years. In addition to being in need of a new caregiver, these children also had to overcome the loss of their primary caregiver from whom they had moved away. Some of the children may also have moved more than once, as the first placement of foster children in Norway often is in an emergency shelter home where the child stays until a suitable foster home is provided. These factors may have created a vulnerability and disruption in the development of attachment that may be observed as internalizing symptoms such as withdrawal, emotional reactivity and anxiousness.

It is also probable that in this group the foster parents were more aware of signs of internalizing problems than the biological mothers, thus accounting for the reduction of caregiver-rated internalizing problems when the foster children were excluded from the analysis. In Norway, the expectant foster families are selectively recruited and trained in order to provide the foster children with the best possible caregiving environments. Many of the training programs focus on giving the foster parents knowledge in reading children's cues and

non-verbal behavior. A vulnerability caused by both postnatal *and* prenatal risk is also a plausible explanation for the higher levels of caregiver-reported internalizing problems in the foster children.

5.3 Methodological considerations

When conducting research on high-risk population groups, there are some practical implications. In all research, compromises must be made between the “ideal” research standards and pragmatic considerations. Moreover, when doing research on particularly vulnerable clinical groups, extra care must be taken in order to protect the participants and respect their challenging life situation. In the present study, ethical considerations had to be made in order to balance the possible gain in knowledge from research conducted with the potential disadvantages or discomfort to the participants. It was of high importance in the longitudinal study to make every meeting with the participants a positive experience for both the child and caregiver, also in order to make it likely for further participation in the research project. The present study has strengths in the form of multiple comparison groups as well as several follow-up time points. However, although care was taken in the present study to use sound methods, there were methodological challenges in planning and conducting the three studies described in this thesis. As awareness of the methodological challenges are important in interpreting the results, and these challenges are discussed below.

5.3.1 Sample size

As previously mentioned, the somewhat small sample size poses some statistical limitations. With small sample sizes like the present one, the number of covariates entered into the analyses and models are limited. Consequently, controlling for- or demonstrating possible relationships with other variables was not always possible, nor was investigating more complex models of moderating factors such as e.g. the presence of supporting fathers or other adults. The children placed in foster care by age 4½ constituted a subgroup, but the sample size was considered too small to test directly for group differences. The higher rate of internalizing problems and lower birth weight was indicated through the significant differences between the findings from the sensitivity analyses without the foster children.

In addition, statistically significant effects and group differences are more difficult to detect in smaller samples. It is possible that group differences in cognitive functioning at age 4½ years would have been detected in a larger sample size. It is also possible that although there was little prenatal substance exposure, effects of prenatal substance exposure would

have been detected given a larger sample size. Non-significant findings must not be given too much weight in small samples, so it is therefore important when interpreting results in the present study to be careful not to conclude that non-findings are actually conclusive non-findings; absence of evidence must not be understood as evidence of absence (Altman & Bland, 1995). Statistically insignificant findings may be clinically significant and relevant.

5.3.2 Recruitment and selection bias

During the time of the recruitment, clinicians at the residential treatment institutions (for women with substance abuse problems) and the outpatient clinics (for women with mental health problems) were in charge of recruiting the women admitted to treatment to the longitudinal study. The inclusion criteria for the women in the study group were that they were admitted to treatment due to an ongoing substance abuse or a history of substance abuse. This was clearly delineated to the clinicians at the treatment institutions, and to the best of knowledge, this is how it took place. However, some women declined to participate in the study, and five women in the study group withdrew shortly after having been recruited. Those who declined to participate were not systematically registered at the time, and we were unable to document the frequency with which this occurred. The women who declined could not be retrospectively identified, as there is no legal access to any data or characteristics of them. It is possible that both the women who declined and the ones who withdrew, were more vulnerable than the ones who agreed to participate, at least in the risk-groups, and that they maybe did not want to commit to a long-lasting study due to their life situation. In addition, 23 of the women in the study group were voluntarily admitted to residential treatment which may indicate a higher presence of motivation and general resources than other populations of women with substance abuse problems. It is possible that the mothers in the study group were less vulnerable than the general population of mothers with substance abuse problems. This potential selection bias could account for the findings in Papers I and III, and is important to bear in mind when interpreting the results of the study and when generalizing from the results.

5.3.3 Missing data and attrition bias

The attrition rate was relatively high, as is often the case in longitudinal studies of clinical groups. Out of the 83 women and 85 children who were initially recruited, 65 mothers/caregivers and 66 children participated in the 4½-year follow-up. It is possible that the women in the risk groups who managed to create the best conditions for themselves and their children are the women who remained in the study. If so, this could account for the lack

of findings of group differences in cognitive functioning at 4½ years of age. There were also a few missing preschool reports on child social-emotional problems, as some of the mothers in the study group and the high-risk comparison group did not allow the teachers to fill out questionnaires about their children. The reason they gave for this reservation was primarily that they did not wish their child to be identified as someone who potentially had problems. In a small sample such as the present one, it is possible that these missing preschool reports can partly explain the lack of group differences in teacher reported social-emotional functioning. Missing data and attrition bias may account for some of the results, and must be considered when interpreting the results and generalizing from the findings.

5.3.4 Cross-cultural considerations

It is necessary to specify that the detoxification, as it took place in the residential treatment institutions, happened under specially monitored and individually adapted circumstances, most likely highly specific to Norway. Norway is the only country in the world with a legislation that authorizes the detention of pregnant women with an ongoing substance abuse in order to protect the fetus. This study does not say anything about the outcome of detoxification under less controlled circumstances or different conditions. Great caution is warranted when undertaking detoxification, and the current outcomes cannot be assumed to apply to less controlled and supportive settings.

It is preferable to use Norwegian norms whenever possible; even so, for MSEL administered at age 2, and ASEBA applied at age 4½ years, Norwegian norms were not available; consequently, US norms were applied. There is a possibility that with Norwegian norms there would have been slightly different results, and this should be kept in mind.

5.3.5 Objectivity in observation and assessment

It is of general high importance to attempt to secure objectivity in observation and assessment. Lack of objectivity poses a threat to reliability of the instrument used, and thus also to validity.

The use of substances while pregnant was assessed through personal interviews. Hence, it is possible that there was an under-reporting of the use of substances as this may be associated with feelings of shame and guilt. Nonetheless, the women were already in residential institutions due to their substance dependence problems at the time of the interviews, and they were receiving help for their problems. It is therefore less likely that they were under-reporting their substance intake at that time point. When asked about their

substance dependence problems again at the 4½-year assessment, none of the women reported problems with current substance use, but four women reported receiving treatment; three were in OMT at that time, and one mother reported receiving psychological treatment due to recurring thoughts and craving for substances. There is a higher possibility of under-reporting problems with current substance abuse at the 4½-year assessment, as the consequences for admitting substance use at that time would be worse, such as the possibility of losing custody of their children.

When assessing maternal intrusiveness and lack of sensitivity in interaction, two coders who were trained and highly experienced in coding with the PCERA performed the scoring of the interaction pattern. The coders were blind to participant group allocation and were not acquainted with the participants, but were watching video recordings of the interaction. However, the mothers' awareness of being video-recorded may have affected their interaction with their infants, thus possibly creating more positive mother-infant interaction recordings than their regular interaction with their infants.

At the 2-year follow-up, clinicians at the treatment institutions where the mothers had been admitted during pregnancy performed the test of early language skills for nine of the children. The clinicians had been active in the treatment of the women and in further follow-ups of the families after they had been discharged from the institutions. After careful consideration, it was decided that even though the number of participants was reduced, the assessments performed by the clinicians should be excluded from the analyses in order to avoid potential bias in the results. At 4½ years, all the children were tested by test leaders without any relationships to the children or mothers/caregivers. The test situations at both the 2 and 4½ year follow-up were designed to support the child in accomplishing the tasks within a reasonable time limit. Due to practical reasons, the test leaders were not blind to group allocation. During the test situation at 2 and 4½ years, it did happen that a child would lose interest in the task (MSEL and WPPSI-III), become unfocused and wander off. When this occurred, the test leader would decide to take a small break from the task before returning. Although attempting to create equal conditions for every child tested, some children needed more breaks than others in completing the tasks. Whether this occurred more often in the study group than in the comparison groups was not systematically registered or analyzed, and may be important aspects of the test situation, which may have influenced the results. A systematic registration of the number of breaks needed and other challenges during the test situation may be important aspects that should be addressed in future studies.

Another relevant issue concerns whether the caregiver's subjective reports of their children's social-emotional problems observed in the home environment capture "objective" problem behavior, or merely reflect the caregivers' inner representations of their children, thus representing a bias and threat to validity. There were no significant group differences in the preschool teacher's reports of child social-emotional problems, which could lead to an interpretation of the caregivers' reports as being less objective. However, it is likely that the children's behavior is situation-specific and varies between the preschool and home environment (Achenbach et al., 1987), and that the different observers can contribute to information about the child based on the social situation where the child is. It may be better to attempt to understand the caregivers' reports of their children's behavior as reflections of something happening in their social interaction with their children, since the preschool teachers' reports also reflect upon what takes place in their social interactions with the children, and that these reflections depend upon social circumstances.

5.3.6 Direct effects and confounding variables or a complex field and multiple transactions

In experimental research, confounding variables interfering with the relationships of the variables studied pose a threat to internal validity, the degree to which it can be concluded that a treatment variable caused a change in the outcome variable (Shadish, Cook, & Campbell, 2002). Care must be taken to control for possible confounding variables. However, the sample in this thesis was not randomized, as it was not an experimental design, and we did not set out to test for direct effects in any of the studies; instead, we aimed to explore the relationships between relevant variables. Therefore, when controlling for variables traditionally thought of as confounders in Papers II and III (maternal, educational level and single parenthood), the aim was not merely to test only the direct effect of group belonging or other background variables. We also sought to explore to what extent these risk factors play a part in language skills, social-emotional and cognitive functioning in children born to mothers with substance abuse problems. The fact that the observed group differences were not statistically significant when controlling for socio-demographic risk factors, such as single parenthood and lower educational levels, indicates that the socio-demographic risk factors in fact, at least partly, may explain the group differences observed. We cannot, nor did we attempt, to isolate the effect of prenatal substance exposure alone, because it often exists in combination with other risk factors, such as poor maternal education, psychopathology, single parenthood, poor social network and low income. In Norway, it is challenging to match controls on SES at the same time as excluding substance abuse. Mothers with substance abuse problems in Norway

constitute a marginal group with many coexisting risk factors. The present design, in which a high-risk comparison group of mothers with mental health problems was included, attempted to match controls on some risk factors but not on the substance abuse problems. However, the results from the present study indicate that the mothers with substance abuse problems had more coexisting risk factors compared to the high-risk comparison mothers; they were younger, they were more often single mothers and had a lower educational level. In addition did they have higher levels of antisocial personality traits than the high-risk comparison mothers. A transactional model of development seems best suited as a framework in which to interpret the findings of the present study, as it seems that various risk and protective factors in the prenatal and postnatal environment, difficult to disentangle, interacted in determining the functioning in children born to mothers with substance abuse problems.

5.4 Clinical implications

The present study did not aim to test the specific effects of maternal detoxification during pregnancy, but instead aimed to explore the short- and long term functioning of children born to mothers who have received help for their substance abuse problems and how this functioning is associated with relevant risk and protective factors. The findings have some important clinical implications. The children born to mothers with substance abuse problems who were detoxified in pregnancy experienced less prenatal substance exposure and other non-optimal prenatal conditions related to substance use in pregnancy, thereby suggesting a smaller biomedical vulnerability relative to other samples. Furthermore, all these families received support from the CPS, such as financial support and free preschool. The results from the present study indicate that interventions during pregnancy, as well as support after birth, may provide children of mothers with substance abuse problems with a better starting point in life. At the same time, the finding that child birth weight did not catch up with the low-risk comparisons suggests that other prenatal aversive conditions are still present. An early as possible admittance to residential treatment, in addition to supporting the mothers in stopping smoking seem important in order to reduce the risk for lower birth weight. In the short run, the residential treatment may be associated with relatively high financial costs to a society. However, its costs may well balance the costs associated with the alternative options, including the treatment of NAS, but also with hitherto undocumented possible long-term consequences to individuals and society. Although this study cannot isolate the effects of detoxification on perinatal outcome, the overall results suggest that the multi-treatment approach of the residential institutions can account for the differences in perinatal outcome

between the two study groups in Paper I. It is important to recognize that the detoxification in this study took place in residential settings that were maintained throughout pregnancy, and in particularly controlled and supporting environments. It is possible that this close monitoring and individually adapted treatment can account for the success in detoxification.

In addition to having comorbid psychiatric difficulties, the results further show that the mothers with substance abuse problems were more psychosocially disadvantaged compared to the mothers in the two other groups. They were younger, were more often single and had a lower educational level than both the high- and low-risk comparison mothers, and this stayed stable during the 4½ years. Long lasting individualized treatment with each mother tailored to help her with her substance abuse problems, her psychosocial problems, and her underlying psychiatric difficulties such as possible anxiety and depression, combined with therapy targeted at enhancing the mother–infant relationship, is recommended. These interventions are also of importance, in addition to helping these expectant mothers with their substance abuse problems while they are pregnant. This seems to be required in order to enhance the mothers' caregiving capacities and positive interaction with their children. Clinicians working with mothers with substance abuse problems should be aware of the potential negative implications of comorbid psychiatric disorders on caregiving, and the negative influence that maternal insensitive and intrusive behavior in interaction may exert on child language functioning. Furthermore, these families and children are in need of long-term follow-up and support in order to discover and address child social-emotional problems and enhance further positive cognitive development. Financial support and free preschool may be important precursors for later child cognitive functioning, especially in these high-risk families. The children placed in foster care may be in particular need of long-term follow-up, together with their new families.

Although not a subject for the present thesis it is important to recognize that the role of the fathers may be an important treatment issue in families struggling with substance abuse and psychiatric problems. An intervention that includes the father in the treatment and has a focus on improving fathers', as well as mothers' parenting behavior, is also necessary.

Moreover, although not testing transactional processes directly, the results from the present study does lend support to an interpretation of various risk and protective factors in the prenatal and postnatal environment interacting in the development of language skills and social-emotional functioning in children born to mothers with substance abuse problems. From the perspective of a transactional model, interventions are most likely to succeed if they

attempt to reduce the overall burden of risk rather than targeting single risks (Tronick & Beeghly, 1999).

5.5 Future perspectives

This study followed the children born to mothers with substance abuse problems who were detoxified in pregnancy until the age of 4½ years. So far, the results suggest that these children have a smaller biomedical vulnerability and a better starting point in life, which is possibly explained by lower levels of prenatal substance exposure and supportive follow-up relative to other samples of children. There is only a scarce amount of research on the long-time development of children born to mothers who have received help for their substance abuse problems during pregnancy. It is therefore necessary to investigate whether the group differences in the present study will decrease or increase over time. It is possible that more challenges will become evident with adaption to school settings and in the forming of relationships with peers.

There is also a need for more research on the mothers who underwent detoxification. As the results from the present study have shown, the mothers have many disadvantages, as well as a history of substance abuse, and whether and how this changes over time should be investigated.

In this thesis, the fathers' role in their children's development was not assessed, which was due to the high absence of fathers in the study group. Although fathering is a very important issue in current social policy, their role is often not acknowledged in research. Where fathers are considered in substance use-research, the focus is primarily on their negative influence, while their potential positive role as caregivers is often overlooked. Given that the father has received treatment for his substance abuse problems, he can act as the one who vitally contributes in giving the child appropriate care and developmental support (Moe, Brean, Siqveland, & Haabrekke, 2010). The role of the father may be an important factor that ought to be addressed in future studies.

More systematic research on the topics of the present thesis should be carried out with larger samples to substantiate the present findings. With a larger sample size, one could also include possible moderating factors, which would allow for testing and investigating possible transactional processes. Moderating factors such as child individual differences in vulnerability as well as possible protective factors, such as the presence of social support family or friends are some of many important aspects which should be addressed. This could lead to better tailored treatment programs taking into account both risk and protective factors.

6 CONCLUSIONS

Findings from the present study suggest that children born to mothers with substance abuse problems in treatment while pregnant have a smaller biomedical vulnerability and a better starting point in life, possibly explained by lower levels of prenatal substance exposure and supportive follow-up relative to children born to mothers with substance abuse problems who have not received specialized help while pregnant. When 4½ years old, the children born to mothers who had received treatment while pregnant did not score significantly lower on cognitive functioning compared to the low- and high-risk comparison children. It is possible that the residential treatment and further follow-up, as well as financial support and attendance at preschool contributed to- and stimulated a positive cognitive development. At the same time, various postnatal risk factors such as maternal intrusiveness and antisocial personality traits, may contribute negatively to the children's early expressive language functioning. Mothers with a history of substance abuse problems often struggle with problems other than substance abuse, such as single parenthood and lower education, both of which potentially affect their caregiving capacities and their children's early language skills. The children born to mothers with a history of substance abuse problems showed more caregiver-reported social-emotional problems at age 4½ years. Lower birth weight and maternal/caregiver anxiety and depression were both related to child social-emotional functioning; thereby suggesting that aversive prenatal factors other than prolonged prenatal substance exposure as well as caregiver's mental health, are important factors. The findings imply that in addition to optimizing prenatal factors by admittance to residential care units with maternal detoxification and psychosocial treatment as early as possible during pregnancy, mothers with a history of substance abuse and their children are in need of long-term follow-up and support. Rather than targeting single risks, treatment models aiming to reduce the overall burden of risk would seem more likely to succeed. Therefore, interventions with focus on sensitive caregiving and developmental supportive parenting behavior, as well as the caregivers' mental health problems, should be applied in order to promote expressive language skills, enhance further positive cognitive development and prevent development of social-emotional problems in children born to mothers who have received help with their substance abuse problems while pregnant. The results further suggest that the children placed in foster care may be in particular need of long-term follow-up, together with their new families.

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